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THE BLOOD VESSELS OF CHONDROSARCOMAS

by

C. LAGERGREN, Å. LINDBOM and G. SÖDERBERG

An investigation by means of microangiographic and histologic techniques has been carried out on malignant mesenchymal tumors in amputated extremities to establish a basis for their angiographic evaluation. Previous studies of the vessels in fibrosarcomas and osteogenic sarcomas (LAGERGREN et coll. 1960, 1961) have indicated a close agreement between the vascularity and the degree of malignancy. There was only slight, if any, increased vascularization of the tumor compared with that of the surrounding tissue in cases of low malignancy, whereas the great majority of the highly malignant tumors displayed hypervascularization. The present article reports a similar study of chondromatous tumors.

Angiography was performed in 18 cases of chondromatous tumors of the extremities: 16 of these were chondrosarcomas and 2 were chondromas. In 5 of the cases of chondrosarcoma, and in 2 others in which angiography had not been performed prior to amputation, arteriography was carried out on amputation specimens, and these were examined in detail by parallel microangiographic and histologic techniques in the manner described in the previous article.

From the Department of Pathology II (Director: Prof. B. Engfeldt), University of Uppsala, and Roentgendiagnostic Department D (Director: Docent Å. Lindbom), and the Institute of Radiopathology (Director: Prof. L. Santesson), Karolinska Sjukhuset, Stockholm, Sweden.
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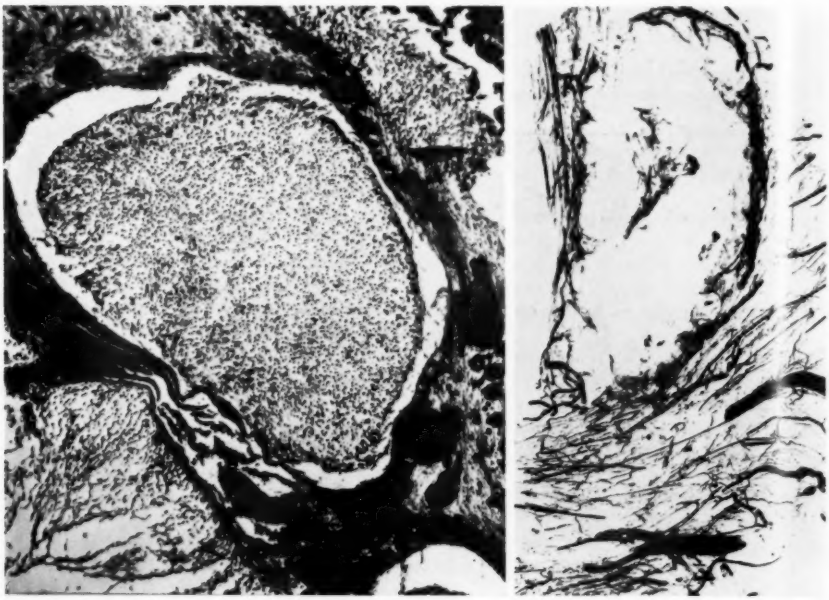

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Fig. 1. Vascular pattern of chondrosarcoma. a) Photomicrograph × 35. Tumor lobule surrounded by wide, irregular thin-walled vessels in interlobular fibrous tissue; in places many narrow vessels. b) Microangiogram × 7. Lobule, for the most part avascular, surrounded by a dense network of vessels.

Findings

Histology. The degree of malignancy in all the tumors was graded according to O'NEAL & ACKERMAN in the same way as in an earlier study of chondrosarcomas (LINDBOM, SÖDERBERG & SPJUT 1961). Out of the 20 tumors examined, 2 were classed as benign chondromas and of the others, which were all chondrosarcomas, 7 were assigned to grade I, 7 to grade II and 4 to grade III. In 2 of the tumors that could be examined as a whole, there was a slight difference in the degree of differentiation, with parts of the tumor corresponding to grade I whereas other parts, often peripheral, corresponded to grade II. These tumors were, of course, finally graded according to their most malignant parts.

The chondromatous tumors had a typical arrangement of vessels, which passed mainly in the connective tissue strands between cartilage lobules (Fig. 1a). The higher the malignancy the more numerous and wider the vessels, these often having very thin walls in relation to their width (Fig. 2). Two types of vessels were found in the chondrosarcoma, one in which the

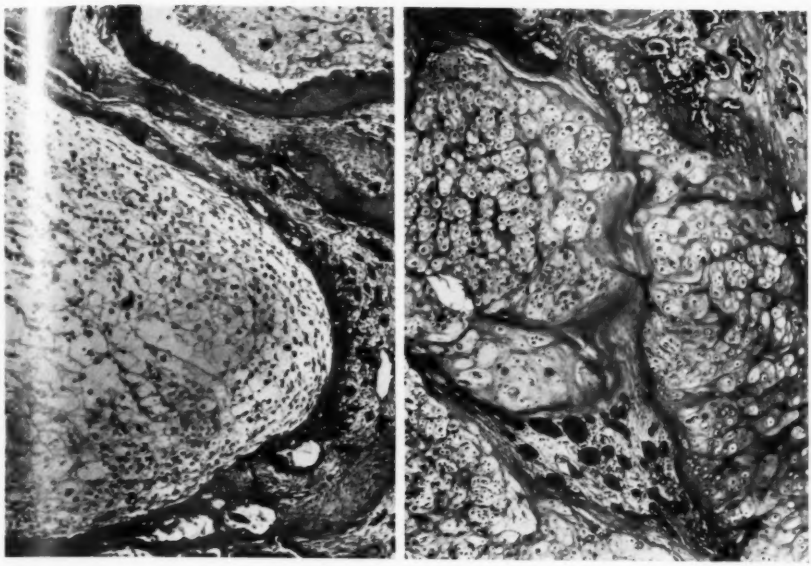

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Fig. 2

Photomicrographs × 35 of contrast-filled specimens, showing the vascularity of chondrosarcomas of different degrees of malignancy: a) grade I, b) grade II and c) grade III.

Most of the vessels contain contrast medium and stand out as dark areas against the tumor tissue. The width, number, and irregularity of the vessels increase with the degree of malignancy.

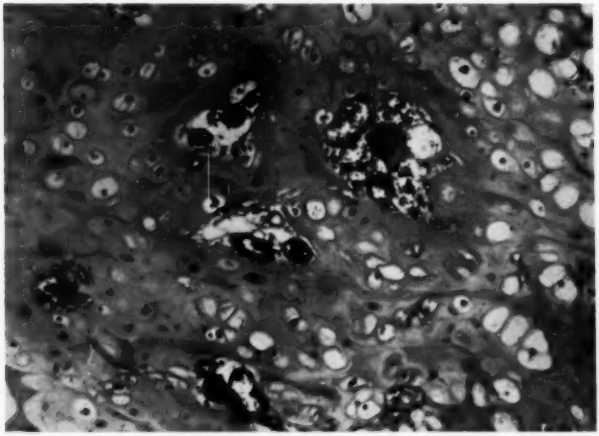

Fig. 3. Photomicrograph × 70 of narrow contrast-filled vessels (width 10 to 50 microns) penetrating into the peripheral parts of a tumor lobule. Chondrosarcoma, grade II.

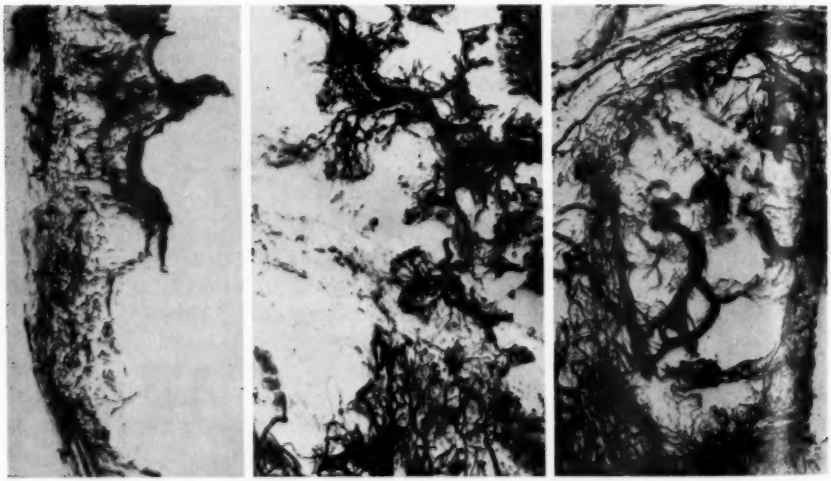

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Fig. 4. Microangiograms × 10 of chondrosarcomas of different degrees of malignancy: a) grade I, b) grade II and c) grade III. The number and width of the vessels increase with the degree of malignancy. The boundary between the neoplastic tissue and the interlobular fibrous tissue containing the vessels is well defined in (a) but increasingly diffuse in (b) and (c) in which large vessels with a brush-like ramification are evident.

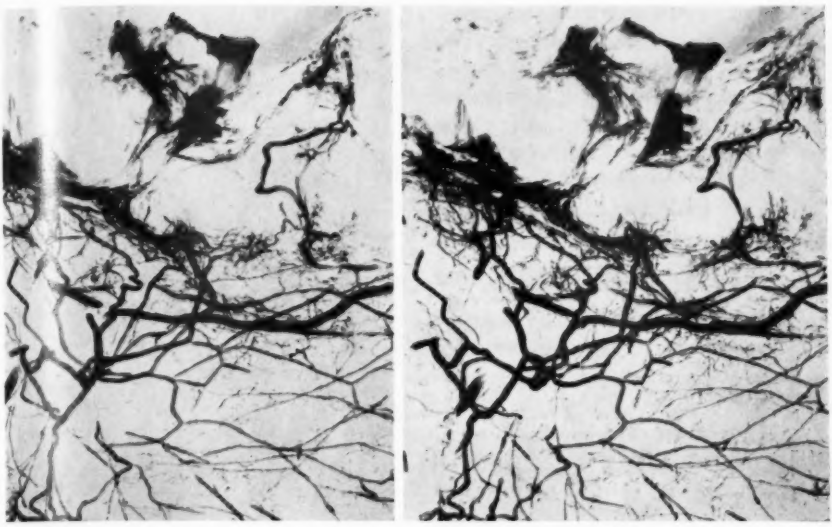

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Fig. 5. Stereoscopic microangiograms × 10 of chondrosarcoma grade II invading femoral head. The vascular pattern of ordinary spongy bone (below) forms a striking contrast to that of the tumor tissue (above). Zone of invasion highly vascular. An artery penetrates for a short distance into the tumor tissue (right upper corner).

vessels were wide and sac-like, often irregular in shape, with very thin walls and 500 to 600 microns in width (Fig. 2c), and the other type consisting of small densely packed vessels with a calibre of 10 to 100 microns (Fig. 2). These fine vessels were predominantly situated in the connective tissue strands between tumor lobuli, but in the less differentiated tumors they showed a tendency to penetrate into the tumor tissue in the peripheral parts of the lobuli with no connective tissue component. In the specimens that had been injected with contrast medium, vessels of down to about 10 microns in diameter were observed (Fig. 3). However, in the actual tumor tissue in the lobuli, some lumina contained erythrocytes, and Heidenhain staining brought out an arrangement of vessels that suggested that the cells were situated in fine capillaries.

Microangiography. The typical arrangement of the vessels in the connective tissue strands between the cartilage lobuli gave these tumors characteristic appearances (Figs 1b and 4). The pattern of the vessels was in marked contrast to that of the surrounding tissue (Figs 5 and 6). The often very wide

Fig. 6. Roentgenogram of a 0.5 cm decalcified section of contrast-filled specimen from a grade III chondrosarcoma of head of humerus. An avascular necrotic part of the tumor, surrounded by invading, highly vascular sarcomatous tissue with a scalloped arrangement of vessels, lies centrally. The tumor stands out clearly by virtue of its hypervascularization.

vessels seemed to be flattened out between the lobuli; some were band-shaped and their lumina were sometimes triangular in section and often varied in appearance. There was, moreover, a characteristic brush-like arrangement of the smaller vessels; from the large interlobular vessels there emerged in places a large number of small vessels, 10 to 100 microns in diameter, with comb- or brush-like arrangements, often running parallel for a short distance into the peripheral zones of the lobuli. This brush-like arrangement of fine vessels was found also in the lower degrees of malignancy but it was considerably more marked in grade III tumors, where they seemed to penetrate more deeply into the cartilage lobuli. The vascularity as evaluated in the microangiograms bore a distinct relationship to the degree of malignancy assessed histologically (Fig. 4).

Angiography. Serial films were obtained in most of the angiographic examinations. Automatic filmchangers were used in some cases so that the passage of the contrast medium through the tumors could be followed more closely. Any increase and widening of the arteries supplying the tumors, the presence of pathologic vessels within the tumors, and shunting of medium through the tumors were recorded in the angiograms. The vascularity of the tumors was graded on the basis of these findings.

Comparison was made between the vascularity and the degree of malignancy. All the grade III tumors were highly vascular and differed from the rest. All the grade I and II tumors were less highly vascularized than those belonging to grade III. The vascularity of the grade I and II tumors varied widely and

Fig. 7. Angiogram in later arterial phase of chondrosarcoma grade III growing in the proximal end of femur with part of the tumor outside the bone. Highly vascular tumor tissue with, in places, a scalloped arrangement of vessels. Some veins already contain contrast medium, indicating an arteriovenous shunt through the tumor tissue.

no obvious difference between the two classes in this respect could be distinguished in the angiograms. In the two chondromas the vascularity was no greater than in the surrounding tissues. The interlobular arrangement of the vessels could be observed in some areas in the grade III cases (Fig. 7).

Discussion and Conclusions

There was a close agreement between the vascularity and the degree of malignancy, with a high degree of malignancy when vessels were abundant in the chondrosarcomas, as in the fibrosarcomas and osteogenic sarcomas. The chondromatous tumors with a low degree of vascularity were more difficult to evaluate; this group contained both benign chondromas and chondrosarcomas of grades I and II. It would therefore appear that poor vascularity does not rule out the possibility of malignancy. The presence of more vessels in a chondromatous tumor than in the surrounding tissues, as seen at angiography, would support a diagnosis of sarcoma. In such cases any biopsy specimens should be taken from the part of the tumor showing the most marked vascularity.

Examination of the vessels in the tumors may prove rewarding in the histologic evaluation of the malignancy of chondrosarcomatous tumors; hypervascularization and the presence of pathologic vessels would indicate malignancy.

Highly malignant chondrosarcomas provide characteristic microangiographic appearances of wide lumina between the cartilage lobuli, giving a scalloped contour to the vascular network; fine, brush-like groups of vessels emerge from the lumina to pass into the peripheral parts of the lobuli. The scalloped contour may also be observed in angiograms, particularly in parts of a

tumor that can be projected free from other structures. The chondrosarcomas of low malignancy are often slow in growth, and in such cases the clinical examination may not suggest malignancy; furthermore, a biopsy specimen may be taken from unrepresentative parts of the tumor and no evidence of malignancy obtained. The treatment of such a tumor may in consequence often be insufficiently radical. If angiography of a chondromatous tumor reveals highly vascular parts, it should be regarded as malignant and dealt with accordingly.

SUMMARY

An investigation of chondrosarcomas by angiographic, microangiographic, and histologic techniques is reported. The characteristic appearances are discussed and the question of treatment considered. Highly vascular tumors were found to be extremely malignant.

ZUSAMMENFASSUNG

Eine Untersuchung von Chondrosarkomen mit angiographischer, mikroangiographischer und histologischer Technik wird berichtet. Das charakteristische Aussehen wird diskutiert und die Behandlung wird besprochen. Sehr gefässreiche Tumoren haben sich als ausserordentlich bösartig erwiesen.

RÉSUMÉ

Les auteurs présentent une étude des chondrosarcomes par les techniques angiographique, microangiographique et histologique. Ils examinent leurs aspects caractéristiques et envisagent la question du traitement. Les tumeurs très vasculaires se sont révélées extrêmement malignes.

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FROM ROENTGENDIAGNOSTIC DEPARTMENT II (DIRECTOR: DOCENT I. WICKBOM), SAHLGRENSKA SJUKHUSET, GOTHENBURG, SWEDEN.

MENINGEAL VESSELS OF THE INTERNAL CAROTID ARTERY AND THEIR ANGIOGRAPHIC SIGNIFICANCE

by

STURE STATTIN

The intracranial dura mater is supplied mainly by the middle meningeal artery, a branch of the external carotid artery which enters the cranial cavity through the foramen spinosum. Other more or less constant branches of the external carotid artery augment the supply. These small vessels arise from the superficial temporal artery, the occipital artery, the ascending pharyngeal artery and from other branches of the external carotid artery and enter the intracranial cavity through the foramina in the base of the skull, through the parietal and condyloid foramina and directly through the calvarium via other small channels. Further small and more constant supply vessels are the accessory meningeal artery, a branch of the maxillary artery, which enters the cranial cavity through the foramen ovale and the posterior meningeal artery which arises from the ascending pharyngeal artery and enters the cranial cavity through the jugular foramen. These supply small areas of the dura near the site of entry and freely anastomose with branches of the middle meningeal artery and other meningeal vessels. Familiarity with these small meningeal arteries is important because an intracranial tumour supplied by the external carotid artery is almost certainly a meningioma. The best method

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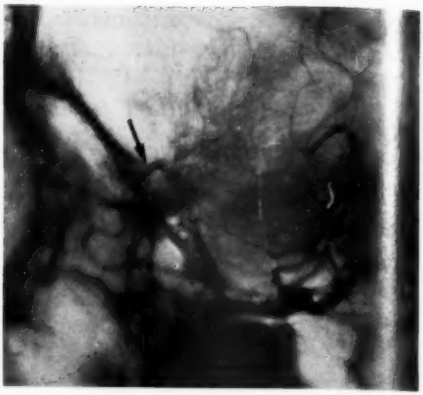

Fig. 1. Olfactory groove meningioma with vascular supply mainly from a hypertrophic anterior meningeal artery ramifying in the tumour in a broom-like fashion.

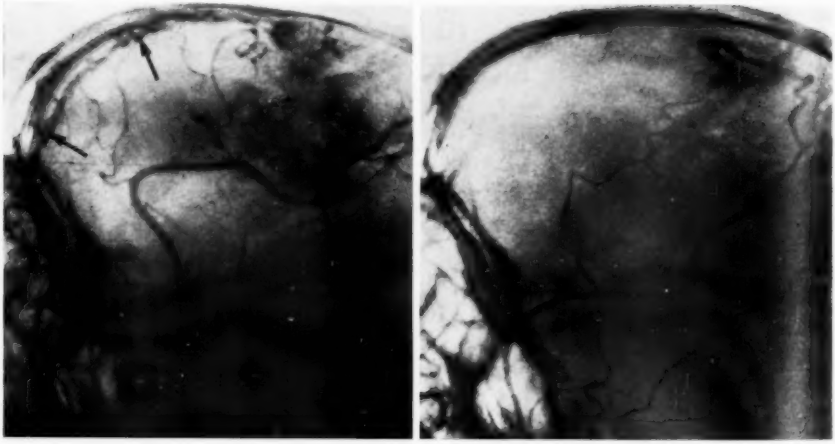

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Fig. 2. a) Meningeal branch of the ophthalmic artery supplying a parasagittal meningioma. b) Same case. Angiography of the external carotid artery.

of demonstrating these vessels angiographically is to inject the contrast medium directly into the external carotid artery. The introduction of the medium into the common carotid artery will often result in an unsatisfactory filling of the external carotid branches; in addition the origin of tumour vessels may not be determined with certainty if the internal and external carotid arteries are both filled at the same time.

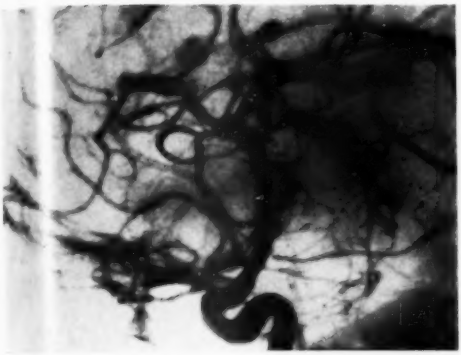

Fig. 3. Internal carotid angiography in a case of meningioma arising in the anterior part of the middle fossa. At operation no vascular supply from the cerebral branches of the carotid artery could be found, and the tumour appeared to be supplied exclusively from the dura by the anterior meningeal artery and other meningeal branches of the ophthalmic artery and the carotid siphon.

Certain areas of the dura are also supplied by vessels from the internal carotid artery. In the anterior fossa the dura draws a part of its blood supply from two branches of the ophthalmic artery, namely the anterior meningeal artery and the recurrent meningeal branch of the ophthalmic artery. In some cases a meningeal branch, which also supplies the anterior fossa, arises directly from the cavernous part of the carotid siphon. The anterior meningeal artery usually arises from the anterior ethmoidal artery shortly after this vessel has entered the anterior cerebral fossa through the anterior ethmoidal foramen; it supplies a small area of the dura of the cribriform plate. The recurrent meningeal branch generally arises from the ophthalmic artery in the optic canal and, passing backwards through the lateral part of the superior orbital fissure, anastomoses with branches of the middle and anterior meningeal artery. The inconstant vessel arising directly from the siphon passes over the lesser wing of the sphenoid and anastomoses with the meningeal vessels mentioned above.

These small meningeal vessels, especially those of the internal carotid artery, have received little attention in the angiographic literature. In normal cases they are very narrow and are only occasionally visible at arteriography. In cases of intracranial meningiomas they may hypertrophy and the angiographic demonstration of such meningeal vessels points to the correct diagnosis (Figs 1, 2 and 3).

The development of the cranial arteries from the primitive branchial arch arteries is very complicated and vessel anomalies in the head and neck are common. Descriptions of such anomalies are abundant in the anatomical literature. For example, the ophthalmic artery or the lacrimal artery may be replaced by branches of the middle meningeal artery. Conversely, branches of the ophthalmic artery may take the place of the middle meningeal artery. We have seen some cases with this latter type of anomaly. The middle meningeal

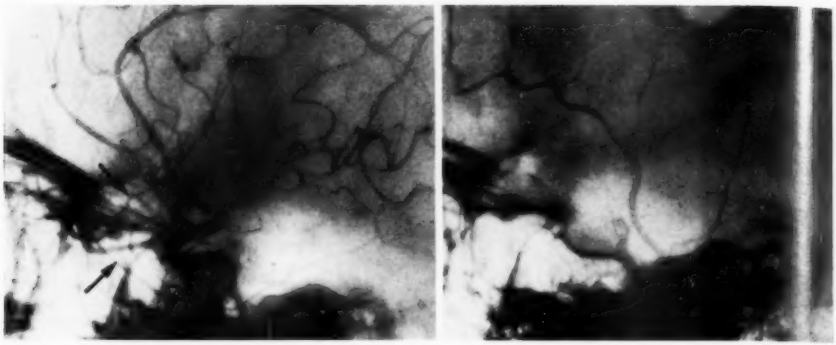

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Fig. 4. a) Anomalous meningeal vessel branches from the ophthalmic artery. The distribution of the vessel is similar to that of the middle meningeal artery. b) Same case. Injection into the external carotid artery. The middle meningeal artery is very narrow.

artery which usually arises from the external carotid artery has been small or missing in all these cases, as has the foramen spinosum, and the anomalous meningeal vessel has arisen from the ophthalmic artery (Figs 4 and 5).

In a paper read at the V Symposium Neuroradiologicum (1957) in Bruxelles we described a vessel which arose from the siphon approximately where the internal carotid artery enters the cavernous sinus and, passing backwards to the tentorium, the vessel contributed to the vascular supply of a tentorial meningioma (WICKBOM & STATTIN 1958, Fig. 7). In their monograph (1957) KRAYENBÜHL and YAŞARGIL illustrate a similar vessel supplying a subtentorial arteriovenous malformation. These authors call this vessel the primitive trigeminal artery. It is however evident that the vessel is not identical with the persistent primitive connection between the basilar artery and the carotid siphon generally called the primitive trigeminal artery (Fig. 6). We have seen this persistent anastomosis in 10 cases, representing 0.2 to 0.3 per cent of our carotid angiographies.

BERNASCONI and CASSINARI (1956) noticed in 5 out of 7 angiographies of tentorial meningioma an unusual, narrow artery which they considered to be of specific value in the recognition of such lesions. It would appear from the illustrations that the vessel was the same one as described by us. FRUGONI et coll. (1960) reported 8 cases of tentorial meningioma, 2 cases of meningioma of the falx, and 1 case of parasagittal meningioma in which they demonstrated the same peculiar vessel. In both these reports the injection of contrast medium was made into the common carotid artery, and the exact origin of the vessel could not be determined. BERNASCONI and CASSINARI suggested that the

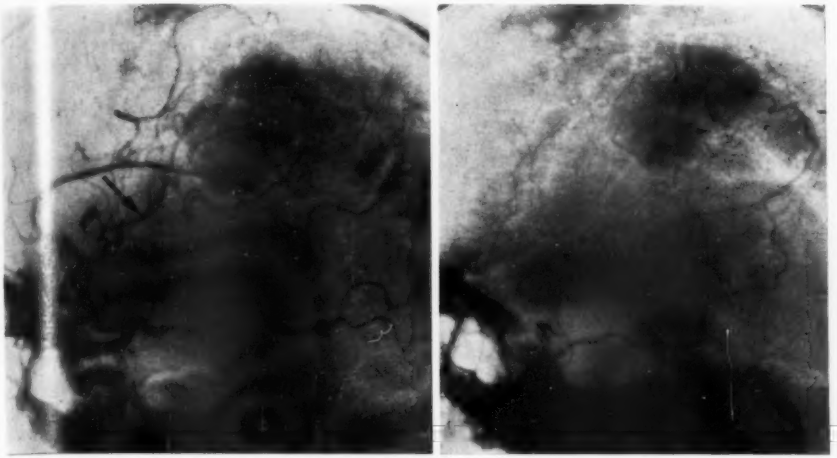

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Fig. 5. a) Hypertrophic anomalous meningeal vessel arising from the ophthalmic artery and supplying a meningioma at the convexity. b) External carotid angiography. The anomalous vessel replaces the middle meningeal artery of the external carotid artery, which is probably absent.

vessel arose from the external carotid artery. In one of the cases reported by FRUGONI et coll. the vessel did not fill when the external carotid artery was injected separately, and considering this fact they had their doubts as to whether the vessel arose from the external carotid artery.

We have seen a meningeal vessel that arose from the intracavernous part of the siphon in 8 out of 10 cases of tentorial meningioma examined with internal carotid angiography (Figs 7 and 8). Of the two cases in which the vessel could not be demonstrated the tumour was located in one case far occipitally, above the tentorium, and in the other case the whole tumour was situated subtentorially. We have also observed a similar vessel in 7 additional nonverified cases. In one of these the vessel together with branches of the posterior cerebral artery supplied an arteriovenous malformation near the pineal body (Fig. 9). In another of the cases the vessel supplied a vascular malformation similar to a cirsoid aneurysm situated in the midline at the anterior attachment of the tentorium. In one of the remaining 5 cases the vessel could be traced to the summit of the tentorium, and in the other 4 cases it could be followed towards the free edge of the tentorium. Superimposed large cells of the petrous bone made it impossible to determine whether the vessel reached the summit of the tentorium or if it terminated earlier. In none of these five cases did any angiomatous vessels fill from the meningeal branch, nor could any rapid passage of medium to the veins be demonstrated. The angiographic

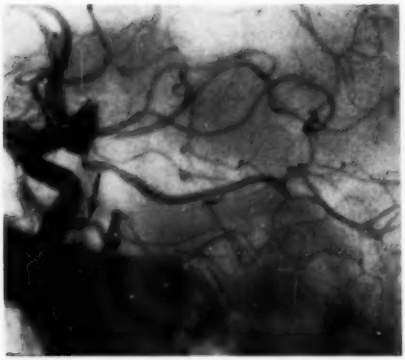

Fig. 6. Persistent primitive connection between the carotid siphon and the basilar artery, generally called the primitive trigeminal artery (arrow).

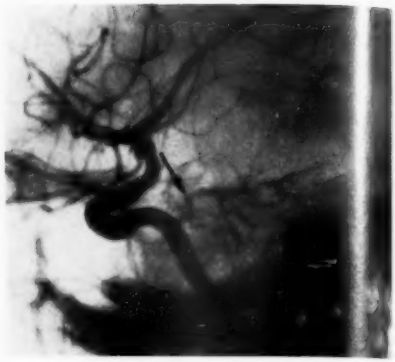

Fig. 7. Meningeal vessel arising from the siphon about where the carotid artery penetrates the outer dura to enter the cavernous sinus. It partly supplies a huge tentorial meningioma.

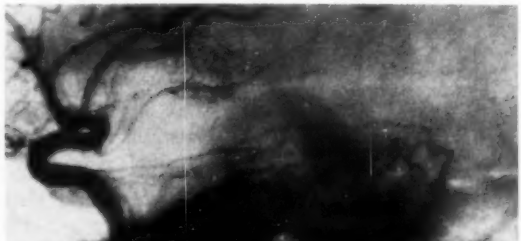

Fig. 8. Meningeal vessels from the siphon supplying a tentorial meningioma.

diagnoses in three cases were as follows: thrombosis of the middle cerebral artery, berry aneurysm of the middle cerebral artery, and complete occlusion of the left and narrowing of the right carotid artery in the neck caused by Buerger's disease; in the latter case there were intracranial vessel anomalies as well. The fourth patient suffered from a hissing noise in the ear synchronous with the pulse, and the fifth had a subarachnoidal hemorrhage but no malformation or aneurysm could be seen on internal carotid angiography.

The meningeal vessel discussed has in some of the cases been observed only in retrospect. The reason probably lies in it having been mistaken for another vessel at the examination. In some cases it may be difficult to distinguish it from a branch of the middle cerebral artery passing basally at the level of

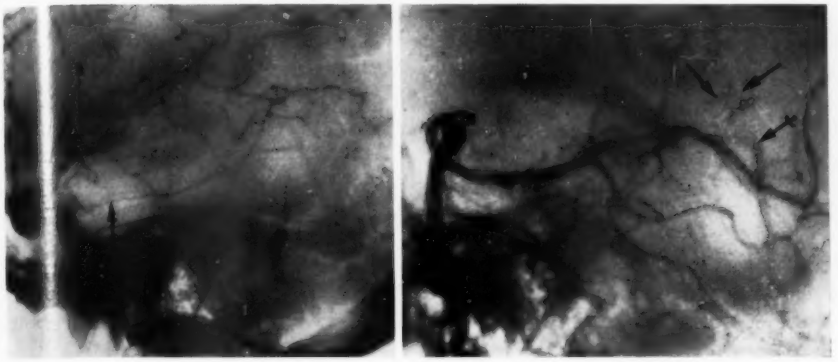

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Fig. 9. A meningeal branch from the siphon supplying an arteriovenous malformation near the pineal body. No operation performed. b) Same case. Vertebral angiography. Rapid passage of medium from the malformation (←) to the straight sinus (↔).

the siphon or sometimes crossing the latter. The anomalous meningeal artery of the ophthalmic artery mentioned earlier may also appear to come off from the carotid siphon.

We have not been able to find any description in the anatomical literature of the meningeal vessel we described. In order to find out if the vessel may exist normally we have examined about twenty cadavers, some in cooperation with Dr. Schnürer at the department of pathology. A number of cases were examined with the aid of a special microdissection technique, after injection of a water-soluble dye into the internal carotid artery, and in three of these cases we have found a very narrow vessel arising from the siphon in the region where the internal carotid artery enters the cavernous sinus. After passing backwards the vessel ramified in the anterior part of the tentorium, anastomosing with other meningeal vessels to this region. No such vessel was found in the other cases; this might be due to imperfect technique but it might also be that the vessel was missing. It seems however reasonable to assume that the vessel may exist normally as an inconstant meningeal branch of the internal carotid artery, which in some cases contributes to the vascular supply of the tentorium. The chances of seeing this narrow vessel at clinical angiography in normal patients are rather limited. Pathologic lesions rich in vessels involving the tentorial region, such as meningiomas of the tentorium and clivus, and arteriovenous malformations in the neighbourhood of the tentorium demanding an increased blood supply, may cause this meningeal vessel to hypertrophy, which markedly increases the chances of demonstrating it angiographically.

The demonstration of meningeal vessels is of importance in lesions believed to be meningiomas or arteriovenous malformations, since a tumour blood supply from such vessels strongly indicates that the tumour is a meningioma, and a complete outline of the blood supply of a vessel malformation will be of considerable value in any operative procedure. It must be kept in mind that meningeal vessels arise also from the internal carotid artery. Internal carotid angiography should be performed, even if a tumour which appears to be a meningioma is situated entirely in the posterior fossa, as our experience which is supported by that of FRUGONI et coll. seems to indicate that most tentorial meningiomas obtain a blood supply from a meningeal vessel arising from the carotid siphon. It is our intention to continue our study of the variations in the meningeal vascular supply, especially of those from the internal carotid artery.

SUMMARY

The vascular supply of the intracranial dura is discussed with special reference to normal and anomalous meningeal branches of the internal carotid artery. A very narrow meningeal artery arising from the siphon and ramifying in the tentorium may exist normally, although it will probably be demonstrable at clinical angiography only when hypertrophied and supplying a lesion rich in vessels.

ZUSAMMENFASSUNG

Die Gefässversorgung der intrakraniellen Dura wird mit besonderer Bezugnahme auf die normalen und aberranten meningealen Zweige der A. carotis interna diskutiert. Eine sehr enge meningeale Arterie, welche vom Siphon aufsteigt und sich im Tentorium verzweigt, kann normal vorkommen, obwohl sie wahrscheinlich bei einer klinischen Angiographie nur dann nachweisbar sein dürfte, wenn sie hypertrophiert ist und eine gefässreiche Erkrankung versorgt.

RÉSUMÉ

L'auteur a étudié la vascularisation artérielle de la dure-mère intracranienne, et en particulier, les branches méningées normales et anormales de l'artère carotide interne. Il peut exister normalement une très fine artère méningée provenant du siphon et se ramifiant dans la tente du cervelet; cependant, il ne doit être possible de la mettre en évidence par angiographie clinique que quand elle est hypertrophiée ou quand elle irrigue une lésion richement vascularisée.

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FROM THE UNIVERSITY INSTITUTE FOR EXPERIMENTAL MEDICAL RESEARCH (DIRECTOR: PROF. CARL SEMB), ULLEVÅL HOSPITAL, OSLO, NORWAY.

EXPERIMENTAL ARTERIOVENOUS FISTULAE

by

RAGNAR HOL and RAGNVALD INGEBRIGTSEN

An arteriovenous fistula presents a number of diagnostic, haemodynamic and therapeutic problems. The local haemodynamics of experimental femoral arteriovenous fistulae in dogs, including the possible diagnostic implications, were selected for serial angiographic studies and form the subject of this paper.

Vascularization around an arteriovenous fistula has been explored by many authors and is reported to be more abundant than the collaterals which develop following the ligature of a main artery at the same level; the same is true of the progressive arterial dilatation proximal to the fistula.

The blood pressure in the proximal part of the artery is always lowered immediately after the opening of an experimental fistula (NEY, HOLMAN, INGEBRIGTSEN & coll.). INGEBRIGTSEN reported a higher blood pressure in the proximal part of the artery than in the artery of the healthy extremity at a corresponding level in two cases and reviewed three other cases from the literature of congenital fistulae of long standing. The blood pressure in and around the fistula is evidently of importance as a causal factor in the development of the new vascular pattern. The flow to the region is increased and the cardiac output is accordingly augmented, facts which are recognised clinically.

The direction of flow in the artery distal to larger experimental arteriovenous fistulae was found by HOLMAN (1949) to be retrograde; in fistulae in which the length did not exceed that of the arterial diameter, the blood flow in the distal

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artery was in a normal caudad direction. PINOTTI and PUGLIONISI (1955) observed no such retrograde flow in the distal part of the artery in recently established fistulae, measuring 15 to 20 mm in length, although it was present in fistulae of two to three months standing. In femoral arteriovenous fistulae SCHENK et coll. (1957) usually found a 'to-and-fro' flow in the distal part of the artery although usually directed towards the periphery, with no measurable mean pressure value. HENRIE et coll. (1959) examined the effects of large fistulae in the external iliac vessels and reported venous congestion distal to the fistula with reduction of venous oxygen tension and no signs of venous retrograde flow; they noted reduced arterial flow distal to the fistula and inadequacy of the collateral arterial vessels.

INGEBRIGTSEN & WEHN (1960) studied local blood pressure and direction of flow in experimental femoral fistulae; in those in which the slit was 10 to 19 mm in length retrograde flow was observed in the distal part of the artery and a caudad flow in the distal part of the vein immediately after the establishment of the fistula. The circulatory pattern was unchanged after eight to nine months. In those fistulae in which the length of the slit was about equal to the diameter of the artery, the direction of flow in the vessels distal to the fistula was normal, i. e. caudad in the artery and cephalad in the vein. Blood pressure readings from the distal part of the artery and of the vein always showed much higher values on the arterial side, for instance 200/120 against 40/25, in cases with inverted flow in both channels.

Common to both smaller and larger arteriovenous fistulae is the development of surrounding rich vascularization. The size and pathophysiology of the smaller fistulae are however more like those observed clinically; for instance in traumatic arteriovenous fistulae in human subjects the length of the slit is rarely greater than the diameter of the artery.

Material and technique

Eleven adult mongrel dogs with fistulae between the femoral artery and vein were examined. The fistula was established well above the saphenous vessels by suture with thin vascular silk (Lyon floche) and small straight needles (Kirby 16). Six animals had a large fistula with a slit length ranging from 7 to 19 mm and in one dog bilateral fistulae had been formed; in the remaining five dogs a small fistula had been established, usually with a slit length of about 4 mm, i. e. equal to or less than the diameter of the artery.

In the dogs with large fistulae the examination was performed from 3 days to 25 months after the fistulae were made. The smaller fistulae were examined from the 7th to the 63rd day after their establishment; only one fistula was examined twice.

The augmented flow and the increased vascularization in cases with arteriovenous fistulae allow and necessitate a greater dose of contrast medium than

a

b

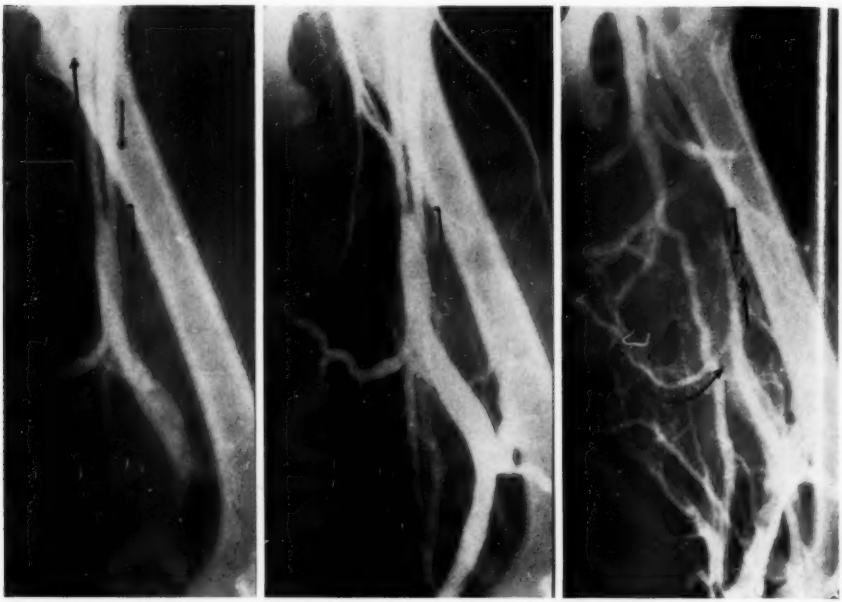
Fig. 1. a) Small fistula 9 days after establishment. Caudad flow in artery and vein distal to fistula with more contrast medium on venous side. Somewhat narrow artery and vein proximal to the fistula, possibly due to oedema. b) 54 days later. Distal part of artery and vein filled simultaneously and equally; the vein is dilated, and more conspicuous collaterals have developed. Fistula reduced in size, proximally a small thrombus. Proximal part of vein still of reduced diameter.

a

b

Fig. 2. Large fistula 18 months after establishment; 0.25 sec between (a) and (b). The distal part of the vein together with the collaterals filled rapidly. The proximal part of the vein is scantily filled and appears to the right of the artery; in this case no narrowing of the vein was observed. The distal part of the artery was not filled in the first films, nor could any reversed flow be observed later.

ordinarily given; the catheter should be of sufficient diameter and the injections made with a pressure injection apparatus. A rapid filmchanger is essential to ensure registration of the fistula with the participating vessels before they are masked by the numerous collaterals and varicosities. About 1 ml Hypaque 45 % per kg bodyweight was injected through a catheter (size P. E. 205) introduced percutaneously via the contralateral femoral artery to the lower part of the abdominal aorta. The injection pressure was 4.5 atmospheres and the first film was obtained at the beginning of the injection. The filmchanger was operated at a speed of four frames per second for the first ten films, the speed then being reduced to two frames per second. In the majority of cases this technique proved satisfactory. In the animal with bilateral fistulae, however, an even larger dose and a more rapid injection of the contrast medium would have been advantageous. As the topography of the fistulae was obvious we had no difficulties in selecting satisfactory projections, and films in one plane were deemed sufficient. Exposure factors: 60 kV, 300 mA, 0.06 sec, 100 cm FFD.



a b c

Fig. 3. Large fistula 10 days after establishment. a) Retrograde filling of the dilated distal part of vein. b) Filling of arterial collaterals proximal to fistula and venous collaterals distal to it. c) Veins in the whole region, together with a widely distributed web of minor arterial collateral branches are well filled. The distal part of the artery is filled cephalad via the arterial collaterals; proximally the contrast medium is wedge-shaped and extends along the whole fistula.

Angiographic appearances

The fistula and the participating vessels. The demonstration of the fistulae was found to depend on the size of the arteriovenous slit. In the cases with smaller fistulae through which the passage was slower and in which the collateral filling occurred later, the fistula was clearly depicted in four to six films; in the cases with larger fistulae and a more rapid circulation through the area, the fistula was observed in one to three films. The contrast density was also correlated to the size of the fistula; when the lesion was large the density was reduced. However, the site of the fistula was always visible as the starting point of the early venous filling (Figs 1, 2, 3 and 5).

The part of the femoral vein distal to the fistula was more obvious than the other vessels in the period after the contrast medium had reached the fistula. In all cases it was dilated, with a caudad direction of flow through incompetent

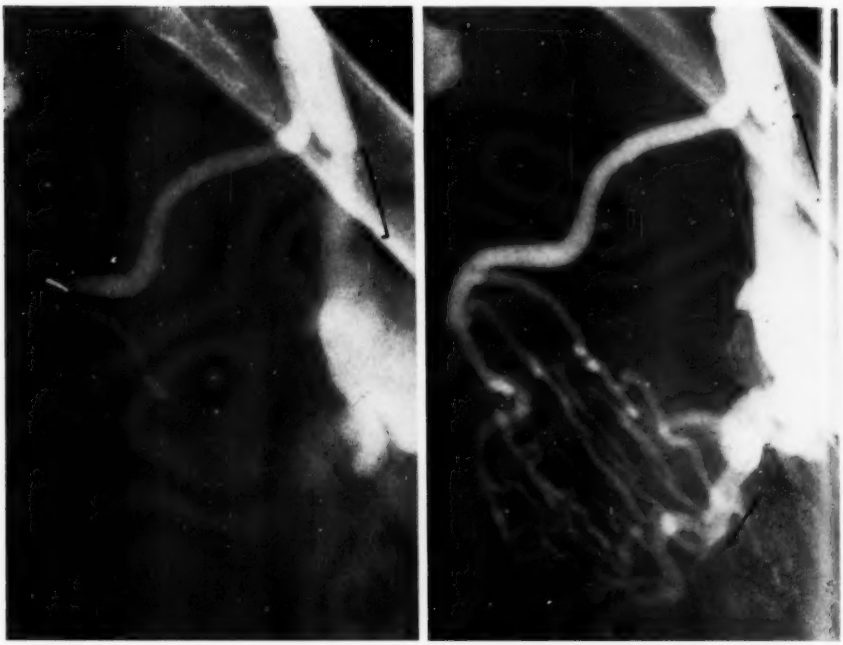
Fig. 4. Large fistula 3 days after establishment. Distal part of vein is thrombosed close to the fistula. The absence of the usual distal venous overflow permits the inverted flow in the distal artery to be observed. Appearances are similar to those seen in arterial occlusion, except for the leakage towards the fistula.

valves, and it usually filled more rapidly and completely than the part of the vein proximal to the fistula. In one case the distal part of the vein was thrombosed and the contrast medium returned through the proximal part of the vein (Fig. 4). The diameter of the vein proximal to the fistula was mostly smaller than that of the corresponding artery and gradually increased proximally, the contrast medium being less dense than in the same vein distal to the fistula. In two cases evidence was found of a small venous thrombus closely proximal to the slit of the fistula; in one of these the diagnosis was confirmed by operation (Fig. 1b).

The filling of the artery distal to the fistula was very different in cases with small fistulae from that observed in cases in which the fistulae were large. The contrast medium in the former cases passed slowly in a caudad direction and in one case intermittent filling occurred, evidently corresponding to the 'to-and-fro' flow reported by SCHENK et coll. When the fistulae were large, no primary filling of the distal part of the artery occurred although the popliteal artery was always filled via arterial collaterals. In half of the animals of this group direct observation of the region of the fistula in the late phase was masked by numerous tortuous vessels throughout the region. The absence of a primary distal artery filling might have been explained by a retrograde flow in these cases; in the remaining cases definite late retrograde filling of the distal part of the artery occurred.

Arterial and venous collaterals. A developed web of collaterals was apparent in all the cases. These were developed partly from branches of the femoral artery and vein and partly from the deep femoral and internal iliac vessels. The branches from these vessels, especially the veins, were wider than normal and, by reason of their tortuosity, were also elongated. The arterial collaterals were filled mainly from arteries proximal to the fistula, while the venous collaterals were filled from veins distal to it.

A close correlation in time between the filling of the arterial and venous collaterals was regularly observed. This correlation was uninfluenced by the

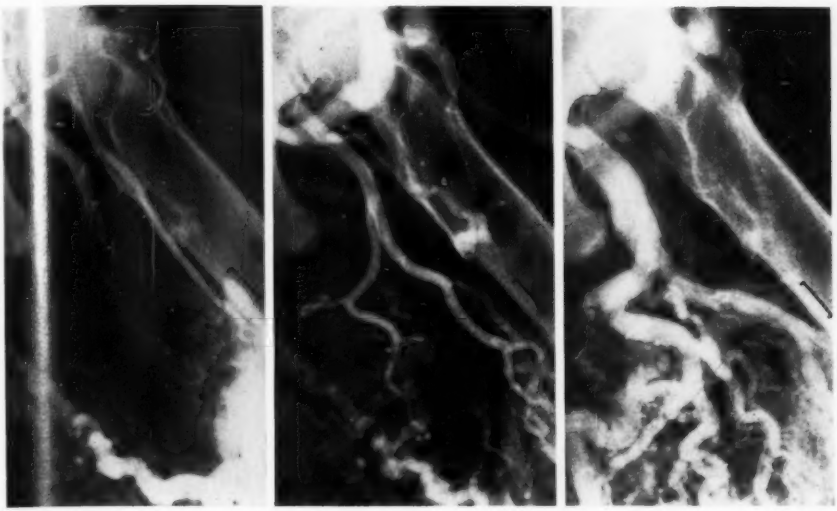


a b

Fig. 5. Large fistula 25 months after establishment. Early filling of single arterial and venous collateral. a) Collaterals filled from their respective arterial and venous origins close to the fistula. b) Filled intermingled web of collaterals. Minute arterial branches proceed distally beyond the web. The venous drainage from the area is shown in fig. 6a, bottom.

size and duration of the lesion and by the rate of flow through the fistula. There thus appears to be no significant difference in the development patterns of the arterial and venous collaterals. The arterial collaterals were less conspicuous than their wider venous counterparts, but were filled with contrast medium earlier than the venous collaterals in the areas proximal to and at the level of the fistula. In cases with large fistulae the distal part of the main artery was filled via the collaterals, while in those with small fistulae the arterial collaterals were seen to contribute more or less to the caudad distal arterial flow. The venous collaterals distal to the fistula were first observed as they drained the distal part of the femoral vein (Figs 3, 6, 7, and 8); the most distal part of the vein had often incompetent valves and hence the venous collaterals drained from a fairly large area.

In one case we had the opportunity of observing a single arterial branch with

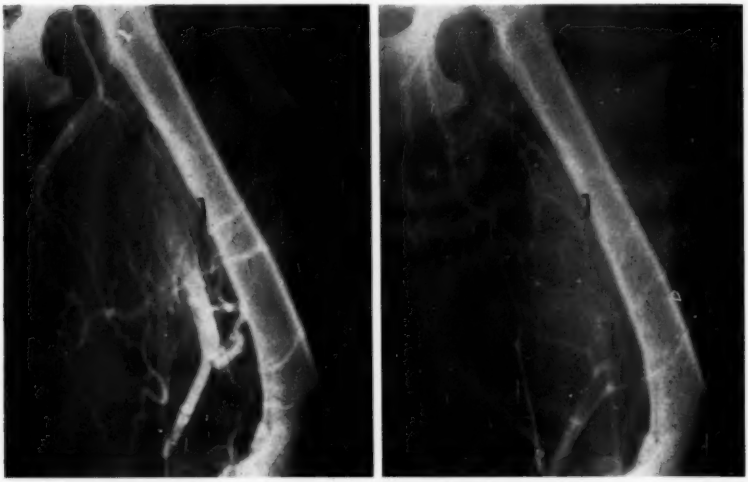


a b c

Fig. 6. Same case as fig. 5. Abundance of collaterals and changing angiographic pattern appearing when the medium has passed the fistula. a) Arterial filling proximal to fistula and venous filling distal to it. b) Better venous filling but arterial filling still present. c) Dominating venous filling but with multiple arterial branches filled distally.

collaterals, together with the corresponding venous branch, to fill with contrast medium before any filling of the other collaterals occurred (Fig. 5). The collaterals were filled from their respective arterial and venous origins and in the first film small arterial collaterals were seen to pass from the vascular web more distally; in later films other veins were draining the area (Fig. 6, bottom).

A further illustration of the development of the collaterals is shown in Fig. 7 in which (a) and (b) are from an examination 9 days after the fistula had been established, 3 and 5 sec respectively after the commencement of the injection; (c) and (d) are from an examination 54 days later, 2.75 and 5 sec respectively after the injection. Some narrowing of the fistula had occurred between the examinations but despite this the circulation was more rapid in the second examination; thus the venous return as shown in (b) occurred after 2.75 sec in the second examination (c). The more distal valves had become competent during the observation time and the venous flow was cephalad in the popliteal region (d); adjacent to the fistula the distal vein had a distal flow as before. Together with the free development of venous collaterals, the narrowing of the fistula may have contributed to this partial re-establishment of normal venous flow.



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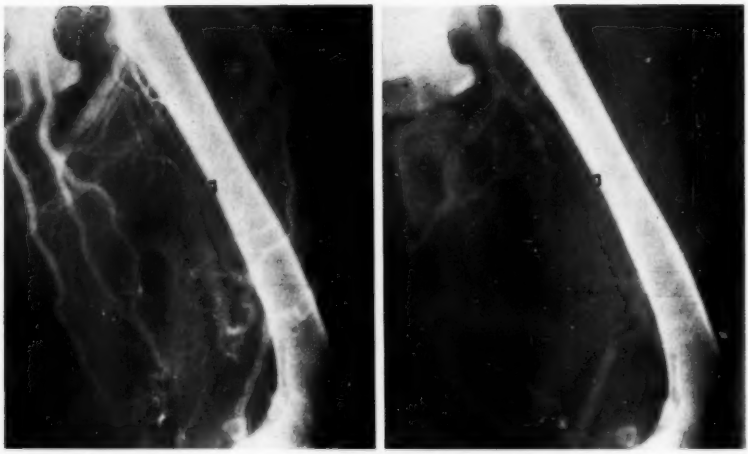
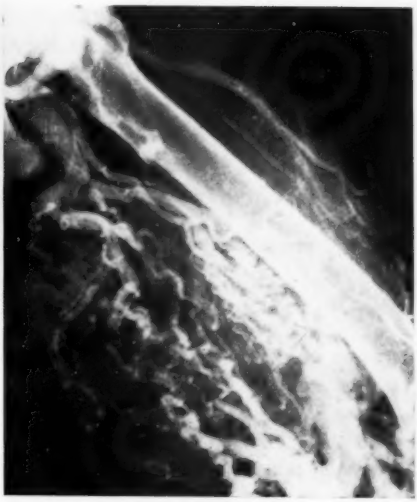


c d

Fig. 7. Same case as fig. 1. Development of collaterals. a) and b) 9 days after establishment of fistula and 3 and 5 sec respectively after start of injection. Slow passage of medium distally in the vein through incompetent valves, with filling of multiple minor collaterals. c) and d) 54 days later and 2.75 and 5 sec respectively after start of injection. The collaterals seen in (b) are already filled after 2.75 sec in (c). In the film obtained 5 sec after start of injection (d) the minor venous collaterals have emptied into the larger veins. The popliteal vein has now competent valves and is filled from the periphery.

a



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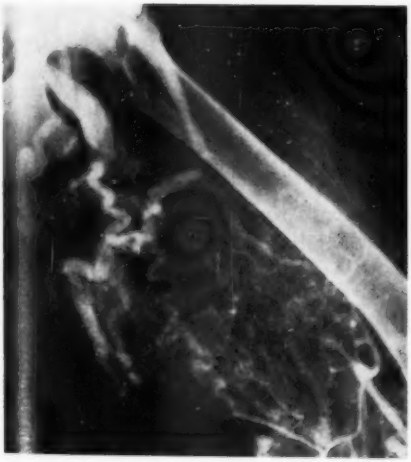

c

Fig. 8. The circulatory phases. Same case as in figs 5 and 6.

a) Second arterial phase, first venous phase and the beginning of the second venous phase.

b) End of second arterial phase, end of the first venous phase, and the second venous phase.

c) Third arterial and second and third venous phases.

The circulatory phases. The changing angiographic pattern of a region with an arteriovenous fistula may often be rather confusing. As mentioned above the vessels were filled with contrast medium with a more or less unchanged correlation in time as regards the collaterals, and this was also true for the main vessels, with the exception of the distal parts of the artery.

The following vascular phases, which are shown schematically in Fig. 9, cover the sequence of events in the filling.

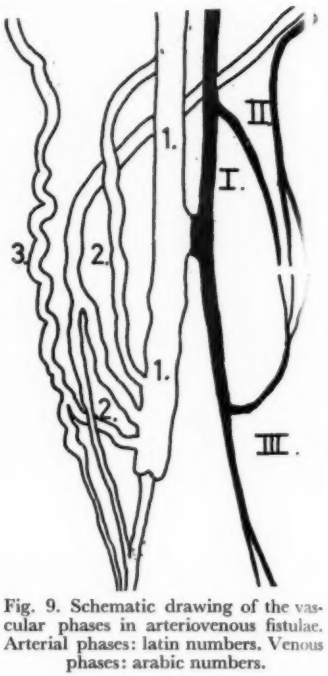

Fig. 9. Schematic drawing of the vascular phases in arteriovenous fistulae. Arterial phases: latin numbers. Venous phases: arabic numbers.

Arterial phases

I. The first arterial phase comprised the rapid filling of the proximal part of the artery and some minor branches arising close to the fistula. A portion of the distal part of the artery was seen filled in cases with small fistulae.

II. In the second arterial phase the contrast medium appeared in the other main arteries to the region (cf. Fig. 8a).

III. The third arterial phase comprised the filling of the arterial collaterals, and in the cases with large fistulae also the filling of the distal part of the artery via the collateral route. In the cases with small fistulae this collateral contribution to the distal arterial flow was not very obvious unless the distal artery flow was slow, or 'to-and-fro'.

Venous phases

1. In the first venous phase the femoral vein was filled in a distal and proximal direction from the fistula (Figs 1, 2, 3b, 7a, and 8a). This phase started shortly after the medium had appeared in the proximal artery and ended towards the middle or completion of the second arterial phase.

2. The second venous phase started as soon as some branches from the distal part of the femoral vein were filled with medium, and comprised the venous return through collaterals and the draining to larger proximal veins (Figs 2b, 3c, 6 and 8). It started slightly later than the second arterial phase and continued into the third arterial phase.

3. The late filling of the very tortuous superficial veins constitutes a third venous phase (Fig. 8c).

Discussion

Angiography in human subjects usually demonstrates numerous collaterals and regional venous overflow in arteriovenous fistulae. The demonstration of the fistula itself may be difficult possibly due to the presence of minute or multiple fistulae, or both. Furthermore the vascular topography may be more complex

tha in the experimental artificial fistulae between a major artery and vein. In the present investigation the technical problems were less when the fistulae wer small, whereas the importance of rapid injection and film changing was mos evident in the larger fistulae. A careful observation of the arterial and ven us phases might be an aid in finding the correct exposure timing for den onstration of the fistula in clinical cases.

Our observations are valid only for communications between a major artery and vein. Similar changes will, however, presumably be found in fistulae between smaller vessels or vessels of different calibre. Our investigation would appear to show that apart from the increased flow through the main artery to the region there will also be an augmented flow in the adjacent arteries, as judged from the development of arterial collaterals. This contribution to the distal part of the artery is more important when the fistula is large. The distal arterial flow is then inverted and consequently the collaterals are supplying with arterial blood, not only the region distal to the fistula, but also the distal part of the main artery with its leakage towards the fistula. Thus, flowmetric recordings in the proximal part of the artery will not give the total amount of increased load on the circulatory system in arteriovenous fistulae, and the values will be less correct in larger fistulae than in smaller ones.

The angiographic findings correspond well with the pressure readings and flowmetric recordings in the cited literature. As pointed out by HOLMAN and INGEBRIGTSEN & WEHN the direction of flow in the vessels distal to a femoral arteriovenous fistula depends upon the size of the latter; when the length of the slit was larger than the diameter of the artery, we found evidence of inverted arterial flow. We never observed a normal flow direction in the distal part of the vein as observed by INGEBRIGTSEN and WEHN in dogs with smaller fistulae. Their observation may possibly be explained by difference in the size of the slit in their cases and in the present series of small fistulae. In all the present cases the venous valves distal to the fistula were found to be incompetent at least down to the region of the knee; in fistulae smaller than those in our experiments the distal venous valves may remain competent. In one of our cases a spontaneous reduction in the size of the fistula was observed and in this case some distal valves again became competent.

Our constant finding of a reduced size of the vein proximal to the fistula might well be considered as a mechanical attenuation and is in contrast to the observed widening of the vein distal to the fistula. This observation corresponds well, however, to the recording of higher pressure in the distal than in the proximal part of the vein (INGEBRIGTSEN and WEHN). This change in calibre at the site of the fistula might be an aid in localizing the latter in human subjects. The site of the fistula may also be evaluated by observing the filling of the arterial and venous collaterals. The former are filled from branches proximal to the fistula and the latter from veins distal to it.

The films in the present studies were obtained without any consideration

to the amount of radiation. The number of films in clinical examinations in human subjects must necessarily be greatly reduced although the first 3 to 4 exposures should be made in rapid succession at the beginning of the injection of contrast medium.

The arterial topography of the hind limb in dogs differs from that in man in the ease with which arterial collaterals are developed and the manner in which complete ligation of the femoral artery is tolerated. Although the sources for the development of arterial collaterals are more scanty in man, satisfactory vascularization by collaterals may develop following arterial occlusion, and may be far more extensive in cases of arteriovenous fistulae.

Conclusions

Arteriovenous fistulae are better demonstrated when examined with due consideration to the changed haemodynamics, which means with an ample dose contrast medium, rapid injection, and serial roentgenography.

It appears from our series that in cases with a small fistula the distal arterial flow was distad or 'to-and-fro', and the venous flow distad. In cases with a large fistula both the arterial and venous flow was inverted, i. e. cephalad in the artery and distad in the vein. The vein proximal to the fistula was most often narrowed and the distal part always dilated, with evidence of incompetent valves. The arterial and venous collaterals were developed according to the size and age of the fistula. The arterial collaterals were filled from branches proximal to the fistula and the venous collaterals from veins distal to it.

Acknowledgement

We want to express our gratitude towards Prof. J. Frimann-Dahl for his kind permission to use the laboratories of Ullevål Roentgen department for our examinations.

SUMMARY

Eleven dogs with experimental large and small femoral arteriovenous fistulae were examined by angiography. The fistula and the participating vessels, the direction of the blood flow, the development of collaterals and the circulatory phases are described. The possibility of localizing fistulae by the shape of the involved vessels, by the origin of the collaterals and by the circulatory phases is considered.

ZUSAMMENFASSUNG

Es wurden 11 Hunde mit grossen und kleinen experimentell erzeugten femoralen arteriovenösen Fisteln angiographisch untersucht. Die Fistel und die beteiligten Gefässe, die Richtung des Blutstromes, die Entwicklung von Kollateralen sowie die Zirkulationsphasen werden beschrieben. Es wird die Möglichkeit der Lokalisierung von Fisteln aus der Form der beteiligten Gefässe, dem Urspung der Kollateralen und den Zirkulationsphasen besprochen.

RÉSUMÉ

Onze chiens porteurs de grosses et de petites fistules artério-veineuses fémorales expérimentales ont été examinés par angiographie. Les auteurs décrivent la fistule et les vaisseaux qui y participent, la direction du courant sanguin, le développement des collatérales et les phases circulatoires. Ils examinent la possibilité de localiser des fistules d'après la forme des vaisseaux intéressés, d'après l'origine des collatérales et d'après les phases circulatoires.

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FROM THE DEPARTMENT OF RADIOLOGY (DIRECTOR: PROF. H. M. STAUFFER), THE DEPARTMENT OF PHYSIOLOGY (DIRECTOR: PROF. M. J. OPPENHEIMER), AND THE DEPARTMENT OF MEDICAL PHYSICS (DIRECTOR: PROF. G. C. HENNY) OF THE TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PHILADELPHIA, PENNSYLVANIA, U. S. A.

FLOW PATTERN ANALYSIS OF PARTICULATE CONTRAST MATERIAL IN BLOOD VESSELS

Experimental cinefluorography at 260 frames/sec, superimposed oscillography of cardiovascular events, and automatic data reduction

by

José L. Giménez, Barbara L. Carter, George H. Stewart and Peter R. Lynch

More precise and detailed analysis of vascular flow patterns is now possible with newer developments in cinefluorographic techniques. Previously Boehme (1) and Rushmer (9) used cinefluorography to study venae cavae flow patterns but were limited by the relatively slow camera speeds. Extensive studies were also done on the same problem by Brecher (2, 3) using a bristle flow meter; however this technique required considerable surgery. Boehme and Brecher stated that the dominant blood flow occurred in the cavae during ventricular systole. The latter author also noted, as mentioned earlier by Burton-Opitz (4), that the systolic flow became less dominant as the heart rate changed from tachycardia to bradycardia. The results of Rushmer were contradictory to those of Boehme and Brecher so that further study in this area seemed indicated.

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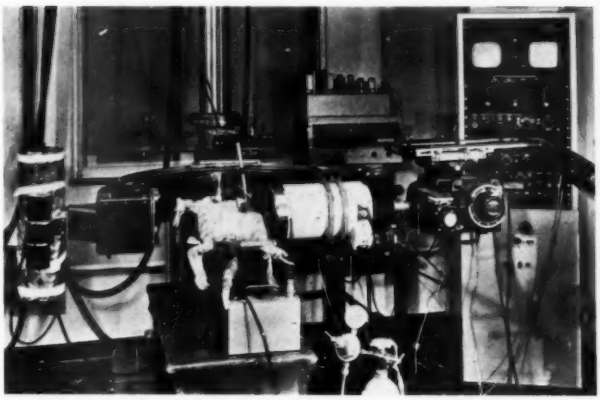

Fig. 1. Cat, with microphone on chest, is inside the 'C' mount which supports the roentgen tube and the Philips image intensifier. The high speed camera is in apposition to the lens of the image intensifier, while its side lens is viewing the oscilloscopic screen on the table behind the 'C' mount.

McDONALD (7) used high speed cinematography to study aortic blood flow by direct transillumination of the artery. Prior to the development of image intensifiers, an impractical high capacity generator with rapid high tension switching would have been required even for experimental animals for direct cinefluorography of the conventional screen at high speeds (250 frames/second). Since image intensifiers increase the brightness of the fluoroscopic screen 500 to 1 500 times, conventional roentgen generators may be used for high speed cinefluorography. The camera used in this study has the advantage of a side lens for taking simultaneous oscilloscopic tracings on the same film, allowing precise timing of the fluoroscopic events.

Flow patterns within the cavae of intact animals have been studied with the above technique (Fig. 1). Since minimal surgery is required, there is little alteration in the normal physiology of these animals. It is the purpose of this paper to elaborate on this technique and to indicate its experimental application.

Image intensifier. A 5-inch Philips image intensifier, equipped with an f/1.5 to 50 mm lens mounted at its focal distance from the output phosphor, was used. The emergent rays were thus approximately parallel. The camera lens, focused at infinity, was brought into apposition with the lens of the image intensifier. A right angle viewer with a partially reflecting pellicle was used for monocular viewing while the cine studies were being obtained. This resulted in a loss of approximately six per cent of the light passing from the image intensifier to the camera (9).

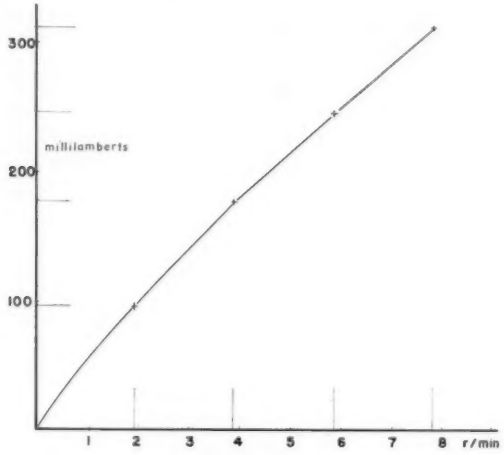

Fig. 2. Brightness of output phosphor versus r/min at intensifier.

The brightness of the output phosphor of this image intensifier was found to be directly proportional to the roentgen at the input screen for a constant kilovoltage (Fig. 2). Using a constant r/min at the surface of the image intensifier, the effect of kilovoltage on the brightness of the output phosphor was evaluated. As shown in the Table below, the intensifier was found to be slightly more efficient with higher kilovoltage. No phantom was used in any of these determinations. An RCA microammeter, used to measure the photocathode current of the image intensifier, served as a brightness control of the output phosphor.

The high speed camera. The Kodak Industrial High Speed Camera is designed for making variable speed motion pictures up to 3 200 frames per second. It was modified to operate reliably at 260 frames per second for this particular project. (The camera was made available and specially modified for this

Table

Effect of kilovoltage on brightness of output phosphor of image intensifier

kVp	HVL in mm Al	Millilamberts for 1 r/min at the intensifier surface
60	1.9	44.9
70	2.0	48.6
80	2.2	51.0
90	2.5	51.7
100	2.7	52.4

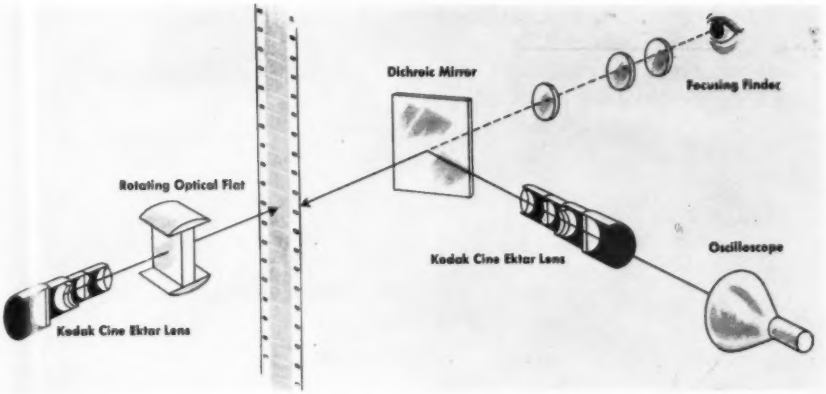

Fig. 3. Diagrammatic sketch of the optical arrangement (Courtesy by Eastman Kodak Co).

application through the courtesy of Eastman Kodak Company, Rochester, N. Y.). The camera is driven by a synchronous motor which operates on 115 volt alternating current. It is equipped with a lamp which flashes time makers along one edge of the film at intervals of 8.3 milliseconds. The camera has two optical systems at right angles. The front lens (Kodak Cine Ektar 25 mm f/1. 9) was used for the fluoroscopic image which, in turn, was refracted through a plane-parallel glass of precise thickness rotating behind the lens as the film traveled downward. The image thus followed the film and was held on it long enough to expose the emulsion. Simultaneous recordings of oscilloscopic tracings were made on this same film through the side lens (Kodak Cine Ektar 63 mm f/2) (Fig. 3).

A Tektronix type 502 'dual beam' oscilloscope with a P-11 phosphor was used. Various parameters such as the blood pressure, heart sounds, ECG and respiration were thus recorded.

Eastman Tri-X Reversal 16 mm film was used and was processed as a negative film with the 'Automatic Minirapid Processor' (Fairchild Camera and Instrument Company, Syosset, New York) using double strength roentgen ray solutions. This unit permits loading in daylight and does not require the use of a leader. A temperature of 80° F with a processing speed of 1 to 1/2 feet per minute was used.

The roentgen source. Four-valve, full-wave rectification was used. In order to minimize the ripple at high intensities, a high voltage condenser of 0.25 microfarads was installed in series with the transformer. The resultant variation in density of the movie films was small enough so as not to be disturbing when the

film was projected in motion. The factors used varied from 75 to 110 kV, [illegible] to 25 mA, with a target-screen distance of 30 inches.

An additional protective device was designed because of the occasional high roentgen exposure. It consisted of a lead-covered work table and a frame supporting overlapping lead strips which surrounded the animal. With the cage in place over a phantom, the following readings were obtained:

kVp	Milli-ampères	Position of ionization chamber	mr per hour
80	10	Observer at image intensifier site	6
80	10	25 cm below intensifier	2.5
80	10	Position of operator adjusting oscilloscope	0.4
80	10	Position of hands of operator at roentgen tube side (injection)	40

A comparative measurement with the ionization chamber 52 cm lateral to the field yielded the following results: 50 mr per hour with no phantom in place, 160 mr per hour with phantom in place, 26 mr per hour with protective frame placed over the phantom.

Data reduction from film. The films were projected with a Kodak Analyst at 16 frames per second for a general survey of the dynamic events. Frame-by-frame analysis was then done with a Vanguard Motion Analyzer (Vanguard Instrument Corporation, Roosevelt, New York), a model which provided precise ten diameter magnification of the movie film projected on a ground-glass screen (Fig. 4). This analyzer is equipped with adjustable hair-line X and Y coordinates superimposed on the projected image and a frame counter. The projection head can be rotated 360° to align angular motions on the projected image with either of the coordinates. Data can be extracted directly from the device or converted to electrical digital form by means of commercially available analog-to-digital converters or 'digitizers'. Once in digital form, the data can be recorded on punch cards, magnetic tape or any other form desired for further processing.

For this particular project the Vanguard Analyzer has been modified in several ways to facilitate the reduction of data. Electric analog readout of the Y coordinate and frame count has been added. This permits the direct plotting of one axis of displacement versus film frames or time on a standard electronic X—Y plotter. To provide Y-axis analog readout, a 40-turn potentiometer has been coupled to the Y axis cursor drive through anti-backlash gearing. Suitable scale factor and zero adjustments as well as a mercury battery supply have been included. To provide the time analog signal, a 40-turn potentiometer is directly coupled to a stepping motor which is driven synchronously with the film advance motor. Thus with each film frame advance, the motor and potentiometer move ahead one step. Suitable scale factor, zero adjustment and mercury battery power have been provided.

Fig. 4. Equipment for analysis of film. Left to right: Vanguard Motion Analyzer, control panel and X—Y Variplotter.

Since some motions were relatively slow, analysis of every frame was unnecessary and systematic sampling proved adequate. To facilitate this procedure the Vanguard film advance circuit was modified to automatically move the film a certain number of frames. An advance of 1, 2, 3, 4, 6, 8, 12 or 24 frames can be selected on a front panel switch. Additional modifications were incorporated to make a dot on the graph by momentarily dropping the pen on the X—Y plotter. This sequence of events was initiated by a push-button on the analyzer.

The net result of the modification was to enable a single operator to quickly reduce the film data to a series of dots on the graph paper which are a plot of single axis displacements versus time (Fig. 5). Once in this form, the data can be additionally processed to obtain the velocity and acceleration of the motion. For this, the X—Y plotter becomes a function generator. An accessory unit will automatically follow a properly prepared curve giving an electrical analog of displacement versus time. This signal may be singly or doubly differentiated by a simple computer circuit to give the velocity or acceleration of the motion. This must be plotted on a second X—Y plotter.

Accuracy of the system. The basic accuracy of this data system must be considered in several parts. One is the inherent error of the equipment in analyzing displacement of droplets vs time. A lead rule milled precisely at one centimeter intervals was placed in the same location as the animal and cineradiographic recordings were obtained. These centimeter intervals were then reduced to a series of dots on graphic paper using the Vanguard projector and

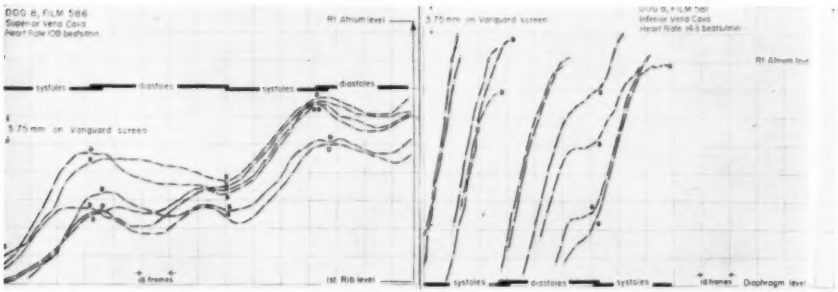

Fig. 5. a) Superior vena cava tracings as recorded through the X—Y Variplotter. 1 mm on Vanguard screen equals 1.59 mm at mid-sagittal plane of experimental animal. 1 frame equals 3.84 milliseconds. b) Inferior vena cava tracings as recorded through the X—Y Variplotter. Conversion factors same as in (a).

the Variplotter. Four investigators each made five sets of curves to determine individual discrepancies and variation from one person to another. With this approach, all static system errors from the roentgen source to the graph paper were included. The total error was found to be too small to evaluate quantitatively. Errors due to roentgen ray geometry (variation in magnification) and resolution were also minimal, though of greater magnitude than that of the system itself. The accuracy of the time coordinate when using power line frequency as the standard had very little error.

A second consideration is the method of recording the droplet movement. Studies of motion blurring and of light persistence with image intensifiers have shown that the initial rate of decrease in light intensity is so rapid that the phosphor 'lag' does not interfere with the usefulness of photographic exposures of two milliseconds or less per frame in 'stopping' rapid motion with high speed cinefluorography. Motion unsharpness due to the frame rate of the camera has been evaluated by photographing a rotating disc (10). Blurring was found to be negligible at the rate of 260 frames per second and with linear velocities up to 120 cm/second.

The third consideration is related to the determination of velocity, the slope of the curve recorded on the Variplotter. A special protractor was calibrated for reading the velocity in cm/sec directly from the slope of the curve. The accuracy depends on the ability of the operator to match this protractor with the curve. The error in per cent of reading is given by the expression:

$$\% \text{ error} = \left[\frac{\tan(\alpha \pm \Delta)}{\tan \alpha} - 1\right] \times 100$$

Δ = error in reading true angle (degrees)
α = true angle

he error is small for slopes of less than one but as the slope increases above or the error increases rapidly. By appropriate choice of scale factors, the slope can be reduced to minimize this error.

Experimental application

RANKLIN and JANKER (5), BOEHME (1) and RUSHMER (9) have used cinefluorography to study flow patterns of contrast material within the venae cavae of intact animals. The equipment described in this paper allows a more complete and concise analysis of these flow patterns. The movement of particulate contrast material in the inferior and superior vena cava was recorded by the high speed movie camera with simultaneous cardiac parameters from the oscilloscope. Subsequent frame-by-frame analysis was used to correlate caval flow pattern with various cardiac events. Lipiodol and ethiodol droplets, the majority measuring 2 mm in diameter, or CO_2 bubbles (8) were used as contrast material. The movement of these small droplets gave an indication of blood flow in the vessels. The range of the velocities was 4 to 60 cm/sec.

Comparisons in flow pattern between bradycardia and tachycardia have been studied in cats and dogs. It was found that the droplets in the superior vena cava moved 2 to 3 times slower than those in the inferior vena cava. As has been shown in previous investigations, a difference was noted between tachycardia and bradycardia in the superior vena cava; with tachycardia, the droplets moved forward during systole but stopped or moved retrograde during diastole (Fig. 5a). These studies have shown a different flow pattern in the inferior vena cava (Fig. 5b), the droplets moving forward both during systole and diastole. The difference between the two cavae was not as apparent with bradycardia; both showed forward movement with systole and diastole. A detailed presentation of these physiologic studies appears elsewhere (6).

Acknowledgements

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SUMMARY

High speed cinefluorography at 260 frames per second with simultaneous oscilloscopic tracings has been used in the study of caval flow patterns in animals. The equipment and the method for concise analysis of film records including automatic data reduction are described. Analysis of droplet movement has revealed a difference in the flow pattern between the superior and inferior venae cavae during tachycardia and bradycardia.

ZUSAMMENFASSUNG

Kinefluorographie mit 260 Bildern pro Sek. mit gleichzeitiger oscillographischer Kontrolle ist beim Studium des Blutflusses in der V. cava bei Tieren benutzt worden. Die Ausrüstung sowie die Methode für genaue Analyse der Filmstreifen einschliesslich automatischer Datareduktion werden beschrieben. Die Analyse von Tröpfchenbewegungen hat einen Unterschied im Blutfluss zwischen der V. cava superior und der V. cava inferior während einer Tachykardie und einer Bradykardie aufgezeigt.

RÉSUMÉ

Les auteurs ont utilisé la cinéradiographie rapide à 260 images par seconde avec enregistrements oscillographiques simultanés pour étudier la circulation cave sur des animaux. Ils décrivent l'appareillage et la méthode d'analyse des enregistrements sur film, avec réduction automatique des données. L'analyse du mouvement de gouttelettes a montré une différence de type de débit circulatoire entre les veines caves supérieure et inférieure au cours de la tachycardie et de la bradycardie.

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FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. KNUT LINDBLOM),
KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN.

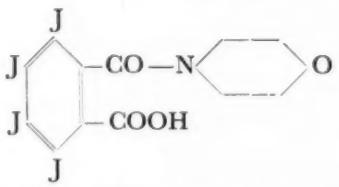
EXCRETION IN THE BILE AND URINE OF A BILIARY TRACT CONTRAST MEDIUM

An experimental study in the rabbit

by

JAAN NOVEK

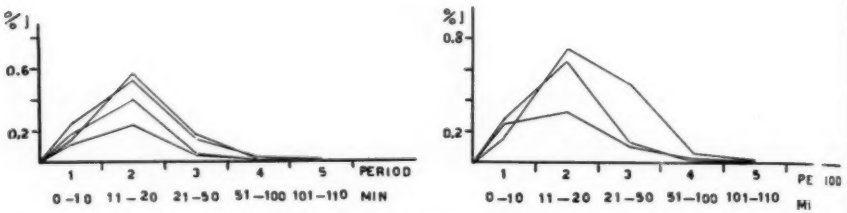
Of a series of iodized compounds prepared by SKAGIUS & EKEMARK the N-methyl glucamine salt of 3, 4, 5, 6-tetra-iodophthalic acid morpholide (Ph 761/3, see formula below) showed very promising properties as a roentgen



Formula of 3, 4, 5, 6-tetra-iodophthalic acid morpholide.

contrast medium. The gallbladder filled rapidly when the medium was given intravenously in preliminary tests in the rabbit. Since its acute toxicity in earlier experiments had appeared to be low (2 g/kg mice) the compound was selected for further study. A closer investigation of the toxicity of the substance (EDLUND & ZETTERGREN) have however made it clear that the compound is not suitable for clinical use.

Submitted for publication 19 September 1960.



Diagrams 1 and 2. Iodine concentration in the choledochal bile after doses of Ph 761/3 of respecti ely 0.06 and 0.11 g/kg bodyweight.

The excretion in the bile and urine of the contrast medium was studied in the rabbit and the results are now presented. An earlier series of experiments with Biligrafin in the rabbit (NOVEK 1959) served as control material.

Technique. The rabbits were not deprived of food or water. Laparotomy and duodenotomy were performed under mebumal anaesthesia and a polythene tube (No. Pe 160), 17 cm in length, was introduced into the common bile duct; the cystic duct was not ligated. In the males, the urinary bladder was emptied by catheterization just before the start of the experiment. In the females, the bladder was not emptied by aspiration until the end of the experiment; in this group, then, the urine collected was composed of the amount present before the commencement of the experiment as well as that produced during its course. At the conclusion of the experiment, the gallbladder was excised and the gross appearances of the liver and kidneys were noted. Only healthy animals are included in the report.

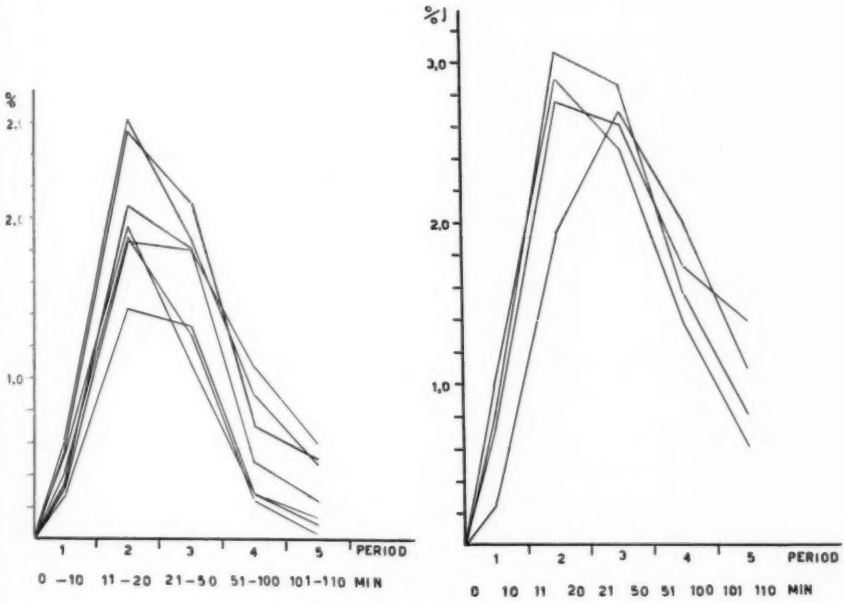
The bile flow during the 10 minutes preceding the injection of the contrast medium was taken as a control sample. When the injections had been completed, the bile was collected during the following standard periods: 0—10, 11—20, 21—50, 51—100 and 101—110 minutes.

The experimental animals comprised 18 rabbits. Four of them were given 0.06 g/kg, three 0.11 g/kg, seven 0.32 g/kg, and four 0.56 g/kg bodyweight Ph 761/3.

Results

The concentration of iodine in the bile was analysed after injection of the different doses of Ph 761/3 (Diagrams 1 to 4). A dose of 0.06 g/kg bodyweight gave the highest iodine concentration of between 0.24 and 0.57 per cent; after a dose of 0.11 g/kg the highest concentration of iodine ranged from 0.33 to 0.73 per cent. The maximum values obtained with a dose of 0.32 g/kg bodyweight lay between 1.43 and 2.62 per cent, and with 0.56 g/kg between 2.70 and 3.06 per cent iodine. With one exception, the highest iodine concentration was recorded in the 11—20 min period. In the exception, the peak value was not recorded until the 21—50 min period; the bile flow during the first interval in this instance was appreciably lower than in the other experiments in this series.

Initially Ph 761/3 always reduced the bile flow. The fall was noted promptly after the injection of the contrast medium and amounted on the average to



Diagrams 3 and 4. Iodine concentration in the choledochal bile after doses of Ph 761/3 of respectively 0.32 and 0.56 g/kg bodyweight.

between 50 and 70 per cent, although the individual variations were wide. The reduction in flow was not related to the size of the dose. The initial decrease was in some instances followed by a temporary slight increase in flow. This increase was not accompanied by any reduction in the iodine concentration; thus the admixture of gallbladder bile was unlikely.

The percentage excretion as measured in the common duct was fairly uniform and ranged from 12 to 24 per cent after doses of 0.06 and 0.11 g/kg bodyweight. The excretion also varied little after doses of 0.32 and 0.56 g/kg bodyweight, and ranged from 21 to 34 per cent.

The contents of the gallbladder were examined in 9 cases. A dose of 0.11 g/kg, for instance, gave a concentration of between 0.10 and 0.40 per cent iodine, while an iodine concentration of between 1.35 and 2.64 per cent was recorded after a dose of 0.56 g/kg body weight. The iodine concentration in the gallbladder was as a rule higher than the mean iodine concentration in the choledochal bile within 110 minutes. At the conclusion of the experiment, between 0.08 and 3.85 per cent of the contrast medium injected was recovered from the gallbladder.

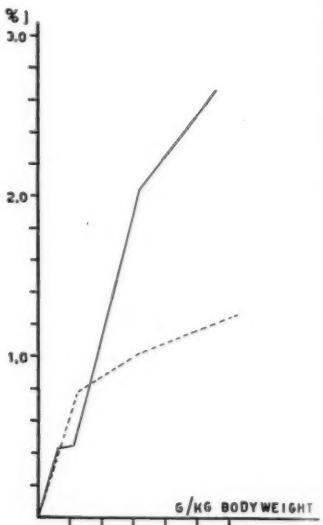


Diagram 5. The mean maximum iodine concentration after different doses of Ph 761/3 (—) and Biligrafin (.....).

The excretion in the urine was examined in 12 cases. In two instances the urinary volume was fractionated. This showed the iodine concentration to reach its highest values in the latter half of the experiment. The percentage excretion following doses of 0.06 and 0.11 g/kg varied between 30 and 65 per cent, and after doses of 0.32 and 0.56 g/kg bodyweight between 13 and 49 per cent.

Discussion and Conclusions

The mean maximum iodine concentration in the choledochal bile was 0.43 per cent after a dose of 0.06 g/kg and 0.57 per cent after a dose of 0.11 g/kg bodyweight. A dose of 0.32 g/kg gave an iodine concentration of 2.05 per cent, and one of 0.56 g/kg gave 2.67 per cent iodine. The iodine concentration in the choledochal bile was thus greatly dependent upon the size of the dose. Doses of both 0.06 g/kg and 0.11 g/kg of Ph 761/3 gave lower iodine concentrations in the choledochal bile than 0.12 g/kg of Biligrafin. However, the highest dosage of Ph 761/3 gave up to twice the iodine concentration produced by Biligrafin (Diagram 5). Further, a dose of approximately 0.15 g/kg of Ph 761/3 was estimated to give an iodine concentration equal to that of a similar dose of Biligrafin.

The highest iodine concentration following the administration of Ph 761/3 was regularly recorded in the 11—20 min period. With Biligrafin, the highest values were noted in different intervals depending upon the dosage.

The percentage excretion in the bile of Ph 761/3 differed from that of Biligrafin. Increasing doses of Ph 761/3 led to an increasing excretion of the medium, while with Biligrafin the excretion diminished; even large doses of Ph 761/3 never led to excretion so high as that following small doses of Biligrafin.

The total excretion in the bile and urine of Ph 761/3 within a period of 110 minutes was good and ranged from 40 to 80 per cent.

Acknowledgement

The author would like to thank Mr Kurt Skagius, Ph. D., of AB Pharmacia, Uppsala, for his valuable advice and help in compiling the analytical data. The author is also indebted to this firm for the financial aid and iodine analyses which made the study possible.

SUMMARY

The excretion in the bile and urine of an experimental biliary tract intravenous contrast medium was studied in healthy rabbits under mebumal anaesthesia. This medium gave iodine concentrations in the choledochal bile that were up to twice those given by Biligrafin, and the total excretion was good.

ZUSAMMENFASSUNG

Die Ausscheidung eines experimentellen intravenösen Mittels für das Gallengebiet in die Galle und in den Urin wurde an gesunden Kaninchen in Mebumalnarkose studiert. Dieses Mittel gab eine Jodkonzentration in den Gallengängen die bis zu zweimal grösser war als die, welche man mit Biligraphin erhält, und die totale Ausscheidung war gut.

RÉSUMÉ

L'auteur a étudié chez des lapins sains sous anesthésie au mebumal l'excrétion biliaire et urinaire d'un moyen de contraste biliaire expérimental administré par voie intraveineuse. Ce moyen de contraste a donné dans la bile cholédocienne des concentrations d'iode s'élevant jusqu'au double de celles données par le Biligrafin, et l'excrétion totale a été bonne.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROF. GREGERS THOMSEN), RIGS-HOSPITALET (UNIVERSITY HOSPITAL), COPENHAGEN, DENMARK.

DISSECTION OF THE AORTIC WALL IN RETROGRADE LUMBAR AORTOGRAPHY

by

C. E. GUDBJERG and JAN CHRISTENSEN

Injury to the arterial wall with subsequent intramural deposition of contrast medium is now a well-known complication of direct percutaneous lumbar aortography and was first reported by GAYLIS & LAWS in 1956. In a comprehensive review of 13 207 lumbar aortographies from 301 clinics in U. S. A. the incidence of this complication was reported to vary from 1 to 20 per cent. The available literature appears, however, to contain no collected survey on the incidence of intimal injury caused by percutaneous retrograde aortography using the catheter technique of SELDINGER with insertion of the catheter via the femoral artery. We therefore reviewed all abdominal aortographies performed in our department during the period 1953—1959 with a view to assessing the frequency of this type of injury. The material comprised 451 investigations. The distribution according to technique, and indication, with the incidence of intimal damage, in brackets, was as indicated below:

Technique	Indication	Number of cases
Retrograde	Arteriosclerosis	126 (36)
	Other diseases	293 (0)
Direct	Arteriosclerosis	31 (6)
	Other diseases	1 (0)
	Totals	451 (42)

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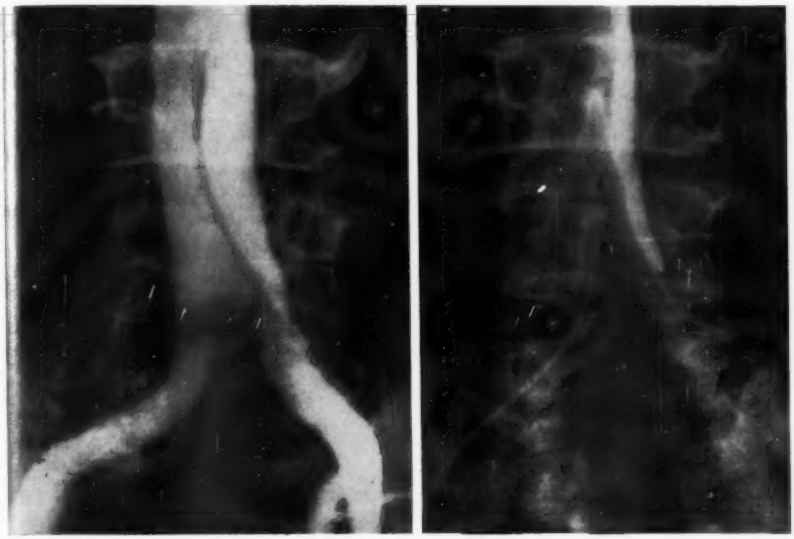


a b

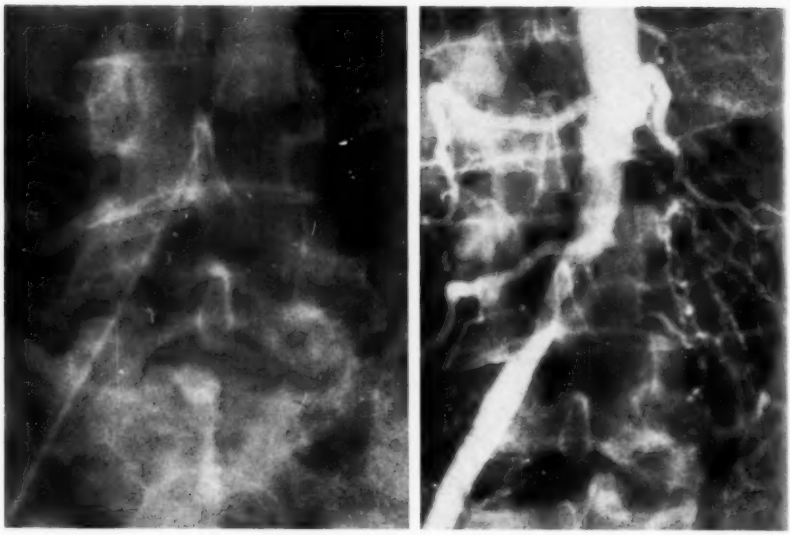
Fig. 1. a) 2 sec after injection of contrast medium. Arcuate filling defect in the distal part of the aorta. b) 10 sec later. A deposit of contrast medium still remains in the vascular wall.

The injuries occurred only in patients examined for probable circulatory disturbances in the lower limbs due to arteriosclerosis.

The aortographic appearances of an intimal injury generally consist of a sharply defined, arcuate filling defect with a subintimal deposition of contrast medium, the latter being an almost constant finding in all the films. The deposit was found in most of the cases to have persisted after the remainder of the contrast medium had left the blood stream (Fig. 1). Less commonly and when the injury is marked, the intramural contrast medium may be spread around the circumference of the vessel for a varying distance (Fig. 2); this was particularly evident in a few cases in which contrast medium was present below large areas of the intima (Figs 3 and 4). A characteristic finding in these cases also was that the appearance throughout the film was constant and unchanged.

Discussion and Conclusion

We demonstrated signs of an intramural deposition of contrast medium in 36 out of 419 aortographies. This corresponds to an incidence of 9 %, exactly the same as that reported in direct lumbar aortography (Boblitt, Figley & Wolfman 1959, McAfee 1957).



a b

Fig. 2. a) Tubular deposition of contrast medium beneath the intima simulating total obstruction. Appearances unchanged in all the films of the series. No collaterals present. b) 2 days later, same technique. No occlusion of the aorta, but thrombosis at the level of the origin of the left common iliac artery.

However, it is important to remember that all the complications in our series occurred in patients with preexisting clinical signs of arterial wall abnormalities. When calculated on the basis of this group of patients alone, the incidence is no less than 29 %. This supports our view regarding the pathogenesis of this injury, viz. that the catheter is caught by an arteriosclerotic plaque, passes beneath it, and then proceeds below the intima for a shorter or longer distance; the injury always occurs in the region of the tip of the catheter from which a major or minor intramural spread of contrast medium is evident. This assumption receives further support from the fact that in 27 out of the 36 cases of damage, there had been difficulties in inserting the catheter (slight resistance to the insertion or inability to pass the catheter to the desired level). That the injection was nevertheless performed appears to have been due to the occurrence of a free reflux of blood from the catheter prior to the injection of the contrast medium and to the contralateral femoral artery not being accessible to puncture.

All the investigations were carried out by the same slightly modified Seldinger technique. The number of intimal injuries was evenly distributed among four different examiners.

Fig. 3. Extensive tubular intramural deposition of contrast medium in the aorta and iliac arteries.

Fig. 4. Marked injury with subintimal spread of contrast medium from the aorta to the femoral artery.

No clinical signs in association with the infliction of the injuries were observed but 7 patients complained of slight pain; 4 of these still had slight low-back pain the next day. The damage should, however, not be neglected since it may contribute to the development of dissecting aneurysm (BOBLITT et coll., MCAFEE).

The deposition of contrast medium beneath the intima may give rise to errors in diagnosis. This applies in particular to cases in which the medium spreads in a tubular fashion beneath large areas of the intima, since this may simulate obstruction due to thrombosis.

Summing up, it may be said that intimal injury is not particularly uncommon but probably involves a risk of untoward sequelae. In the event of resistance to the catheter insertion, therefore, the injection should be performed later or else carried out by the direct percutaneous route.

SUMMARY

The authors report the incidence of intimal injury followed by deposition of contrast medium in the vascular wall in 29 % of cases in a series of 419 retrograde percutaneous abdominal aortographies. This complication was confined to cases of arteriosclerosis and did not occur in other conditions.

ZUSAMMENFASSUNG

Die Autoren berichten über das Vorkommen von Intimaschäden als Folge von Kontrastmittelinjektion in die Gefässwand. Dies geschah in 29 % bei einer Serie von 419 retrograden, perkutanen Aortographien. Diese Komplikation kam nur bei Fällen von Aortasklerose vor.

RÉSUMÉ

Les auteurs signalent la fréquence des lésions de l'intima suivies de dépôt de moyen le contraste dans la paroi vasculaire, dans 29 % des cas d'une série de 419 aortographies rét o-grades percutanées abdominales. Cette complication ne s'est produite que dans les cas d' r-tériosclérose, mais pas dans les autres affections.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROF. ERIK LINDGREN), SERAFIMER-LASARETTET, STOCKHOLM, SWEDEN.

CONVERTIBLE CHAIR-COUCH FOR ROENTGEN EXAMINATIONS

by

ERIK LINDGREN

The development of the Mimer, recently described by FREDZELL & LINDGREN, was prompted by the need for a unit which would offer more facilities in modern neuroradiologic work than the Lysholm skull-table. A need has also been felt for an improvement upon the patient-table. The one employed with the old unit has not been found satisfactory as in practice it permits an examination to be performed with ease only with the subject recumbent, and considerable inconvenience has been connected with its use when the patient had to be examined in the sitting position. The correct procedure in encephalography demands that the patient be examined in the sitting position during the initial stages of the examination but it is also desirable that the change in position from the sitting to the horizontal can be easily performed as the examination proceeds. It may still happen, despite adequate premedication, that a patient faints while sitting upright during an examination, and for this reason it is also important to be able to lower the patient easily and carefully. It would obviously be an advantage, and also minimize the risk of fainting, if the first part of an encephalographic examination could be performed without having the patient sitting upright. Attempts have been made, e. g. by LENZI, to dispense with the sitting position by placing the patient on a more or less

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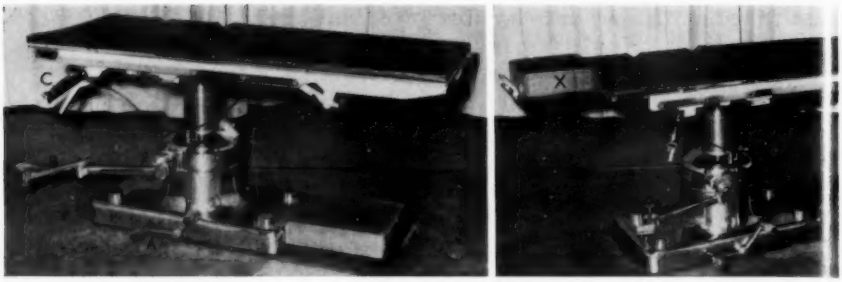

a b

Fig. 1. a) The chair-couch adapted for the recumbent position. A — Foot brake. B — Foot-operated control for raising or lowering the top. C — Handle for the adjustment and locking of the top longitudinally and transversely. D, E, F, G — The four sections of the top of the 'couch' or the parts of the 'chair'. b) The head rest (X) attached.

steeply inclined tilting table. No methods of this type would appear, however, to permit the establishment of a satisfactory encephalography.

Encephalography is probably carried out in most departments in the following manner. The patient is first placed astride an ordinary chair with the arms across its back and the forehead against the skull-table. After the examination in the sitting position has been concluded the patient is transferred to the conventional table for the further stages of the examination. There are many drawbacks attached to this procedure particularly if the patient is unconscious or under general anesthesia.

An examination chair of the kind described by the present author in 1957 was used for some considerable time in the roentgen department of Serafimerlasarettet. The patient was seated in this chair, with rubber-padded supports pushed against the armpits and with further supports for the forearms. The chair, the height of which was adjustable, was placed in front of a Lysholm skull-table, fixed vertically, against which the forehead of the patient rested. A strap could, if necessary, be stretched between the armpit supports to prevent the patient from falling backwards. The patient's feet were placed on a foot rest. The chair proved satisfactory in holding the patient firmly. At the conclusion of the first stage of the examination, the chair, with the patient still in the sitting position, was wheeled over to the ordinary table and placed in such a way that the seat of the chair was at a slightly higher level than the table top; the patient could then be moved over and laid on the table by lowering one of the arm supports of the chair. The seat could remain under the patient as it was readily detachable from the rest of the chair. Although this chair possessed many good points it was not ideal. It may, however, be regarded as a prototype which led to the design and construction of the present convertible chair-couch. DIETRICH

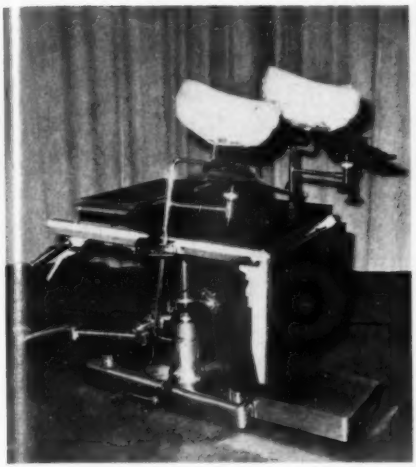

Fig. 2. The convertible chair-couch with arm supports attached and adapted for the sitting position.

Fig. 3. Operator and patient during lumbar puncture; the patient's forehead rests against the vertically fixed object table of the Mimer.

in 1959 described a similarly combined unit, the construction of which was based upon a gynaecologic table. This permitted the patient to sit upright during the first part of the examination and to be lowered to the recumbent position by a few manual adjustments. To judge from the description, however, this unit seems to have many disadvantages.

The general outline and construction of the new examination chair-couch is shown in Fig. 1. It is mounted on small wheels, which lie protected below the base of the unit (and therefore not visible in the photograph), so that it is freely manoeuvrable; the wheels can be locked by means of a foot-operated brake (Fig. 1—A). The unit may also be raised or lowered by means of another foot pedal (Fig. 1—B). When used as a 'couch' the four sections are combined as one unit which can be moved 135 mm longitudinally and 90 mm transversely. Small adjustments in the positioning of the patient in relation to the object table of the Mimer can therefore be effected without having to move the entire unit. The adjustment and locking of the 'couch' top are executed by means of a handle (Fig. 1—C). A head rest may be attached to the head end of the 'couch' if it is found necessary to move the patient, while still on the 'couch', to another location.

The section which represents the foot end of the 'couch' top (see Fig. 1) can be folded down, or the section marked 'D' may be turned up onto the top of section 'E', or again, these two sections may be pulled up together as a unit to form the back of a 'chair' while the patient remains seated on part 'F' of the

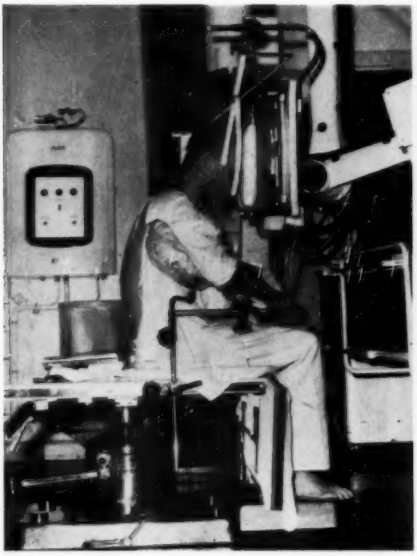

Fig. 4. An unconscious patient in the 'chair'.

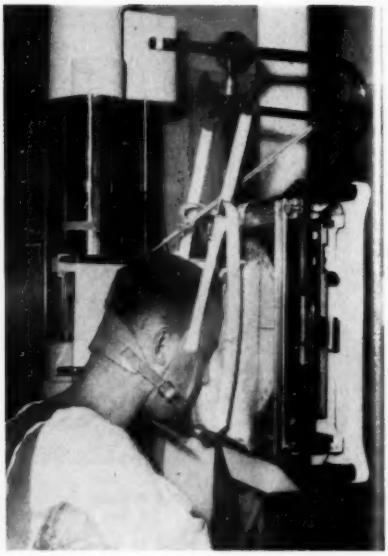

Fig. 5. Details of the fixation attachments for the head.

'chair'. The unit, with arm supports attached and adapted as a 'chair', is shown in Fig. 3; the resemblance to our earlier examination chair is apparent. The supports provided for the armpits and forearms are similar to the previous constructions. They are adjustable both in height and in distance from each other so as to accommodate a patient of any build; the supports are moved in place on rails which are fixed along the edges of the convertible chair-couch.

It will be evident from what has been stated previously that when the unit is used as a chair during an encephalography, the head section is not folded down, as is, for instance, the case with the table described by DIETRICH. The head section in such a position would most likely be in the way of the examiner and hinder his movements when a lumbar puncture has to be performed. Nevertheless the section may still fulfill a purpose by forming a small platform that can be used as an arm rest by the operator making the injection, or for holding kidney bowls or other objects that he may require at hand. The respective positions of the examiner and patient at the commencement of an encephalographic examination are shown in Fig. 3. When that stage of the examination during which the patient has to be in the sitting position has been concluded, the foot section (see Fig. 2—G) is lifted up, section 'D' is moved to the same level as section 'E', and the patient can be laid down.

The device for supporting the head of an unconscious patient (see Fig. 5) is in principle the same as the one earlier described (LINDGREN 1957). This consists of a metal arm that can be mounted at the upper edge of the Mimer object table and upon which another T-shaped adjustable arm is fixed. Straps from the three free ends of the T-arm are attached to a sling constructed like the so-called Glisson sling. This is applied around the neck and the chin of the patient, and by varying the tension of the straps the head of the patient can be bent sideways or flexed to different degrees.

Encephalography in the sitting position, even in the case of a patient who is unconscious, can thus be easily performed with the aid of the new examination unit and the necessary sling attachments. An image intensifier may also be employed if it is considered desirable to study the passage of air. It should be mentioned that the convertible chair-couch may of course be used also with the Lysholm skull-table.

The convertible chair-couch for roentgen examinations is now in production and is being manufactured by Elema-Schönander, Stockholm, Sweden.

SUMMARY

A convertible chair-couch which permits encephalography to be performed as easily with the patient sitting as in the recumbent position is described.

ZUSAMMENFASSUNG

Ein Untersuchungsgerät ‚convertible chair-couch' wird beschrieben. Es ermöglicht, die Encephalographie ebenso leicht mit sitzendem als mit liegendem Patienten durchzuführen.

RÉSUMÉ

Description d'un fauteuil-brancard transformable pour les examens radiologiques, permettant d'exécuter une encéphalographie aussi aisément, que le malade soit en position assise ou couchée.

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FROM THE MEDICAL DIVISION OF THE RESEARCH INSTITUTE OF NATIONAL DEFENCE, DEPT. 1, SUNDBYBERG, AND THE DEPARTMENT OF PHARMACOLOGY, ROYAL VETERINARY COLLEGE, STOCKHOLM, SWEDEN.

DISTRIBUTION OF RADIOCESIUM IN MICE

An autoradiographic study

by

ARNE NELSON, SVEN ULLBERG, HARRY KRISTOFFERSSON and CURT RÖNNBÄCK

Only a few radionuclides, among the great number of fission products produced at nuclear explosions, are of special significance with regard to internal contamination. Cesium 137, apart from strontium 90, is of particular concern because of its long physical half-life of 26.6 years and its high fission yield.

Cesium 137 disintegrates to Ba^{137} of 2.6 min half-life with the emission of two beta particles (92 per cent 0.52 MeV and 8 per cent 1.17 MeV). The lower energy beta particle is followed by a gamma ray of 0.66 MeV. Apart from its physical properties the potential hazard of an internally deposited radionuclide depends upon the period of retention and the distribution in the body. These properties reflect the significance of the element in the metabolism and in turn upon its chemical properties.

Cesium is an alkaline metal belonging to the same group as potassium and rubidium. These three elements have very similar chemical and physical properties. A review of the physiology of rubidium and cesium by REIMAN (1956) cites some evidence for the close similarity of the biologic effects of these ions to those of potassium; significant quantitative differences have been noted, however, between the physiologic behavior of these ions. Cells can distinguish between them and higher organisms will not indefinitely tolerate

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substitution of rubidium and cesium for potassium. It appears from a series of experiments (RELMAN et coll. 1956) that skeletal muscle of rats accumulates the three cations at equilibrium in definite order of preference — cesium > rubidium > potassium. Were rubidium and cesium more abundant in the crust of the earth, there is, according to RELMAN, every reason to believe that they, rather than potassium, would be the chief cations of muscle tissue. The order of preference may be of significance for the estimation of the radiation hazard from cesium 137.

Cesium 137 is often referred to in terms of its danger as an external gamma radiation source. Because cesium 137 is also a beta emitter, it is, however, dangerous as an internal source of radiation. Since the energy which it releases to tissues from its beta radiation is much greater than that absorbed from the gamma radiation, the latter may be neglected for dosage estimation. Consequently the distribution of cesium 137 in the different tissues of the body is clearly a matter of great importance.

The tissue distribution of radionuclides may be investigated either by measuring the radioactivity with a G.M. or scintillation counter in samples of different tissues or by autoradiography. In practically all previous studies of the tissue distribution of radiocesium, impulse counting has been applied. Several investigators (HAMILTON 1947; HOOD & COMAR 1953; BALLOU & THOMPSON 1957; RICHMOND 1958) have studied the distribution of radiocesium in rats at different intervals after administration. It was found that the distribution was similar after oral and intraperitoneal administration. Muscle, skin, gastrointestinal tract and liver were the tissues with the largest cesium accumulation shortly after administration. The concentration in the blood, brain and bone was relatively low. Muscle and brain were unique in that maximum concentrations were not reached on the first day. After the first day the muscle, skin, heart, lungs, testes, and brain contained relatively constant fractions of the total body burden, but the bone, gastrointestinal tract, spleen, liver, kidney, and plasma contained diminishing fractions of the body activity. Erythrocytes contained more cesium than plasma for some time after the first day. On the first day the liver activity represented one-seventh of that in the muscles. A relative decrease of liver activity to only about one-thirtieth occurred after some days.

The transfer of cesium from mother to foetus in rats (HOOD & COMAR 1953) was also studied. The concentration of Cs^{137} in the foetus was nearly constant throughout gestation (0.058 % dose/g) and there was apparently no foetal tissue accumulation.

HOOD and COMAR also investigated cesium distribution in cattle, sheep, and pigs. Muscle showed the highest accumulation followed by the viscera, brain, eye, and endocrine glands. The lowest concentration was seen in the blood, bone, and teeth. The concentrations in various tissues were similar for all species including rats.

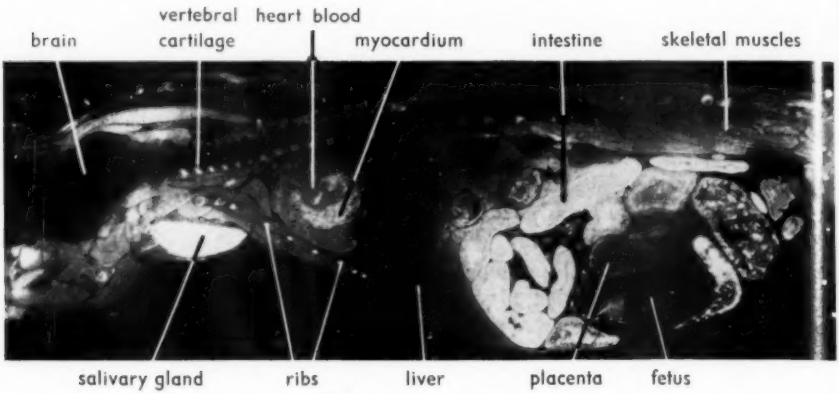


Fig. 1. Autoradiograms showing the distribution of Cs^{137} in a pregnant mouse 5 min after intravenous injection. White areas correspond to high radioactivity. The Cs^{137} concentration is already higher in the myocardium than in the heart blood. High uptake in cartilaginous parts of ribs and vertebrae and in salivary gland and intestine.

Using a macroscopic autoradiographic method (NELSON 1957) the distribution of cesium 137 (NELSON & CARLQVIST 1958) was investigated at different intervals in rats from 5 min to 3 months after an intraperitoneal injection of 40 μC Cs^{137}. A very high density was observed on the autoradiograms at 1 hour over the abdominal organs and heart. No increased density could be seen in the skeleton or teeth. The density on the first day was more even because of an increased density in the muscles. By the third day the density of the muscle was still more prominent although the density of the thyroid and the tongue was about the same. After one month the density, which had decreased considerably in intensity, was most evident in the skeletal muscles.

The macroscopic autoradiographic method did not provide satisfactory information. Hence in the present investigation a method has been used which gives a better resolution and makes it possible to scan the distribution of radiocesium in practically all the tissues, organs and fluids of the body in survey autoradiograms.

Methods. Sixteen mice of the CBA strain, 8 adult males and 8 pregnant females, were injected in a tail vein with carrier-free Cs^{137}-chloride in physiologic saline solution to give an individual dose of about 0.2 μC/g bodyweight.

One mouse of each sex was killed at 5 min, 15 min, 1 hour, 6 hours, 24 hours, 4 days, 16 days, and 36 days after injection by immersion in a mixture of solid carbon dioxide and acetone ($-78°$ C). The female mice were sacrificed 2 days before expected parturition. Sagittal 20 μ sections through the whole

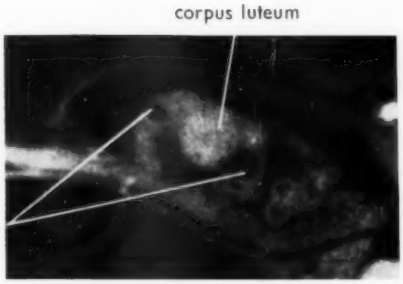


Fig. 2. Detail from autoradiogram showing the ovary 15 min after intravenous injection of Cs^{137} in pregnant mouse. Slight accumulation in corpus luteum.

frozen animals were cut and dried in a freeze room at $-10°$ C. The autoradiographic exposure was made by apposition against Gevaert Dentus Rapid film. The exposure time varied from 7 days for the shortest survival time to 84 days for the longest. The autoradiographic method has been described in detail by ULLBERG (1954, 1958).

Results

Because of the short biologic half-life of radiocesium in mice the overall activity in the tissues decreases rapidly. This has been compensated in our autoradiograms by a gradual increase in exposure time. Satisfactory density was obtained in the autoradiograms from animals sacrificed up to 16 days after the administration of Cs^{137}, while at 32 days the radiocesium content in most tissues gave a very low density.

Shortly after injection the greatest activity is found in the cartilage, salivary glands, kidneys, and intestines. Later, the skeletal muscles and cartilage show the greatest activity.

The distribution in different tissue groups at different intervals will be described below (see also Figs 1 to 7).

Blood. The concentration of radiocesium in blood decreases very rapidly, being lower than in the skeletal muscles by 5 min. This decrease continues, but more slowly, and after 4 days there is scarcely any radioactivity observable in the blood.

Bone, muscle and skin. The compact bone and the teeth show a low radioactivity. A somewhat higher uptake, however, can be observed subperiosteally, especially at the insertion of tendons. A strong accumulation is at all times observed in cartilage and tendons, especially in hyaline cartilage, of the trachea and joints and also in the elastic cartilage of the epiglottis. The fibrous cartilage of the vertebral discs, however, shows a low uptake.

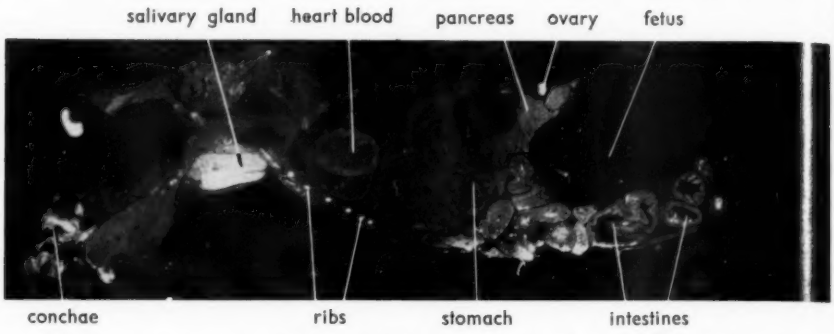


Fig. 3. Autoradiogram showing distribution of Cs^{137} in a pregnant mouse 1 hour after intravenous injection. High radioactivity in ovary.

All skeletal muscles show a great uptake as early as 5 min after injection. The density increases in relation to that in the other tissues, and from one day after injection and onwards the skeletal muscles and cartilage have the greatest cesium contents in the body. There is an uneven distribution between different groups of muscles with the gluteal muscles showing the highest uptake.

The myocardium initially shows a significantly higher activity than the skeletal muscles but by one hour this situation changes and subsequently the density in the myocardium is very low, only slightly higher than the blood level.

The skin and the subcutaneous tissue show a moderately high uptake. A high uptake is observed in the intrafollicular portion of the hair shafts.

Respiratory organs. The respiratory organs show a low activity with the exception of the cartilaginous structures.

Digestive organs. The only specific concentration in the oral activity is in the small mucous glands at the base of the tongue, which have a high activity from one to 24 hours after injection. The salivary glands together with cartilage and the kidneys initially show the highest activity in the body. The accumulation in the salivary glands is very marked by as early as 5 min, and remains so for 4 hours, but is significantly lower after 24 hours. No activity can be observed after 4 days.

The activity in the gastric mucosa and contents is low but in the intestinal mucosa and contents it is high from 15 min to 24 hours after injection. By 5 min there is very high activity in the mucous glands of the colon. From one to 24 hours there is a high activity in the contents of the large intestine followed by a gradual decrease.

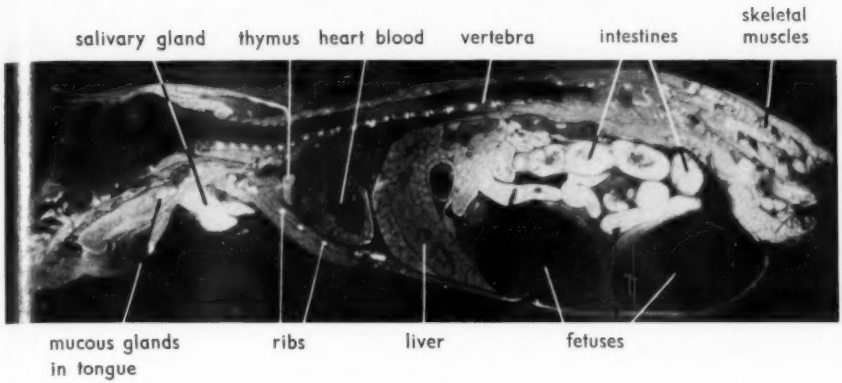


Fig. 4. Autoradiogram showing distribution of Cs^{137} in a pregnant mouse 6 hours after intravenous injection. Concentration in foetuses significantly lower than in the mother.

Pancreas shows the same level of activity as the intestinal mucosa. The islets of Langerhans appear to have a slightly lower activity than the acinar tissue.

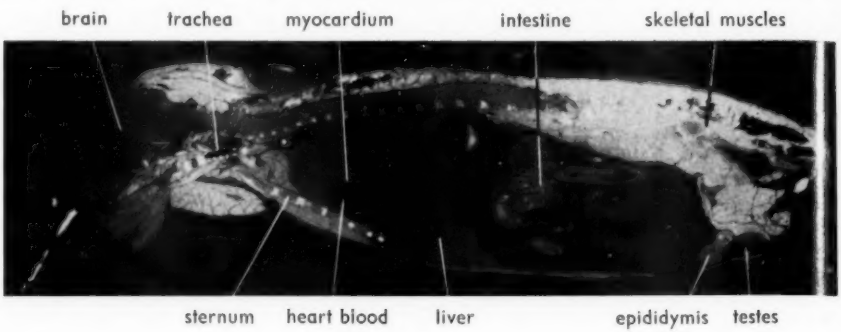
The liver has a consistently low and even concentration of radiocesium. The activity in the biliary ducts at 15 min and 1 hour is slightly higher than in the liver but decreases later.

Urogenital organs. The kidneys show a high activity, from 5 min to 6 hours after injection, with a maximum at 15 min. Subsequently the activity in the kidneys is only slightly higher than that of the liver.

Initially, during the excretory phase, the activity is higher in the renal medulla than in the cortex. The contents of the urinary bladder show a high activity during the first 24 hours.

The testes and epididymis show an even and moderately high activity, slightly higher than the liver, but significantly lower than the skeletal muscles. By 16 days, the radioactivity in the testes is still relatively high (see Fig. 7b). The ovaries of only two mice appeared in the autoradiograms. In one animal killed after 15 min the ovary shows only a moderate activity with the highest uptake in the corpora lutea. No activity, however, is seen in the follicular fluid. In the other mouse, killed after 1 hour, the concentration in the ovary is higher than in any other tissue except cartilage. In this animal the activity is more evenly distributed in the ovary.

Central nervous system. With exception of the blood the brain and spinal cord show the lowest initial radioactivity in the body. Subsequently, however, the activity increases in relation to that in other tissues. The distribution is rela-



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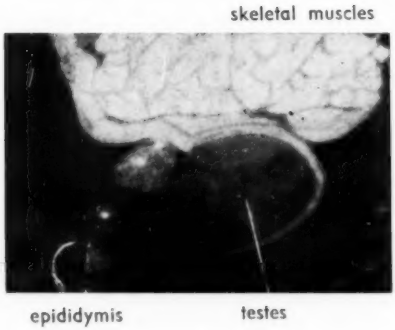

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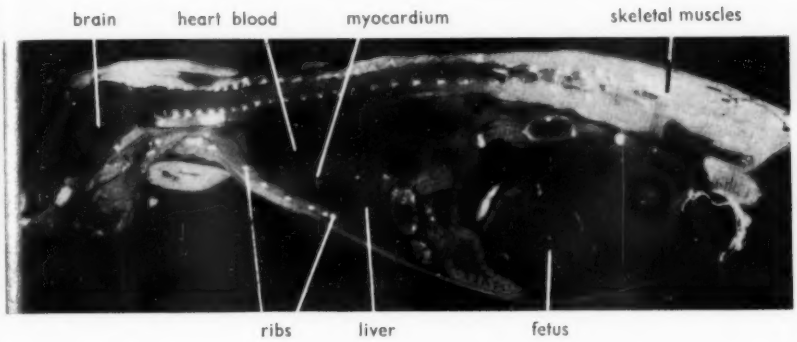
Fig. 5. a) Autoradiogram showing distribution of Cs^{137} in a male mouse 4 days after intravenous injection. b) Detail from autoradiogram in (a).

tively even, the grey matter having a slightly higher activity than the white matter. No accumulation is observed in the choroid plexuses.

Eye. A high uptake is seen in the sclera and the lens and a fairly high in the retina. Unlike the salivary glands the lacrimal glands show no accumulation.

Lymphatic tissues. The activity in lymph nodes, spleen and thymus is slightly greater than in the liver and is evenly distributed. The activity in the thymus of animals killed at 4 days and later appears relatively higher.

Endocrine organs. The activity in the pituitary is only slightly higher than in the brain. The thyroid and the adrenals also show a low activity.



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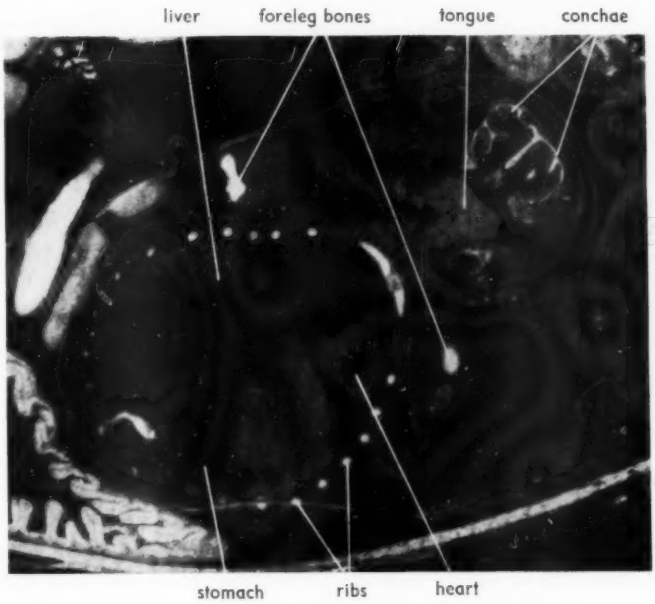

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Fig. 6. a) Autoradiogram showing distribution of Cs^{137} in a pregnant mouse 4 days after intravenous injection. Radiocesium content is now much higher in skeletal muscles than in myocardium. Very low blood concentration. b) Detail from same animal as in (a) showing foetus. Specific uptake in foetal skeleton.

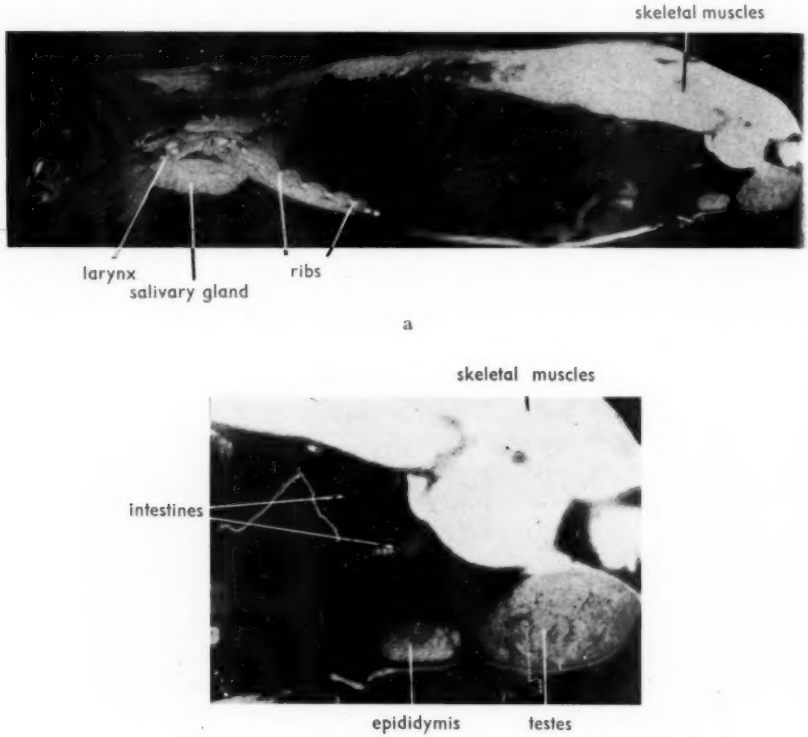

Fig. 7. a) Autoradiogram showing distribution of Cs^{137} in a male mouse 16 days after intravenous injection. Especially high retention in gluteal muscles and cartilage. b) Detail from (a) showing male gonads. Relatively high retention of Cs^{137} in testes.

Foetus. The activity in the foetuses at all intervals is considerably lower than that of the dam. Some foetal uptake, however, can be noticed as early as 5 min after injection. The distribution of the activity in the foetuses including the CNS is relatively even compared with the maternal distribution. No specific accumulation is seen in the foetal skeletal muscles at 16 days. Only the foetal skeleton, especially the tissues developing into definite cartilage, deviates by showing a higher uptake than the other foetal tissues.

Placenta has an even concentration of radiocesium, greater than in the foetus and of about the same level as the liver of the dam. Foetal membranes and fluids show a low activity.

Discussion

Cesium, like potassium, is taken up by the soft tissues against the concentration gradient as already indicated by HOOD and COMAR (1953) and which is generally explained as due to an intracellular accumulation.

The autoradiograms illustrate the rapidity of the disappearance of radiocesium from the blood and the accumulation in the tissues. By as early as 5 min after injection the blood level is lower than in most tissues.

The greatest radioactivity appeared in the cartilage, an observation which does not seem to have been made previously. The uptake was very rapid, which is astonishing with regard to the absence of blood vessels in this tissue. The rapid uptake does not suggest accumulation due to incorporation of cesium into an organic compound. An autoradiographic investigation of the distribution of Na^{22} has also shown a higher accumulation in cartilage than in other tissues (HUGGERT, ODEBLAD, SÖREMARK & ULLBERG 1961). This may indicate that cartilage acts as a cation exchanger. There is otherwise very little similarity in the distribution of Cs^{137} and Na^{22}. The concentration of sodium remains high in the blood, and unlike cesium, sodium accumulates in bone.

With regard to the accumulation in muscles it is remarkable that the myocardium in spite of a high initial concentration does not show the property of the skeletal muscles of retaining cesium. In addition to the tendency to penetrate into cells there must be some other explanation for the distribution in the muscular tissues.

The fact that the foetus, unlike the dam, does not accumulate cesium in salivary glands, kidneys, or intestines may be explained by the low or absent excretory activity in the foetus. The low radioactivity in the foetal muscles, in comparison to that in the maternal muscles, is difficult to explain. The fact that the concentration of cesium in the foetus is lower than that of the mother due to a partial placenta barrier is of importance when evaluating the radiation hazards. This also applies to the fact that the concentration in the testes is not specially high but relatively consistent for a rather long period of time in comparison with other organs. As regards the ovaries our material does not allow definite conclusions. The high accumulation in the ovary in our animals may be explained by the fact that the animal was pregnant.

The uptake in the central nervous system is remarkably low. It is also noteworthy that in our investigation the activity in the liver is always low contrary to what has been reported by some other authors.

Acknowledgement

The authors are indebted to H. Sundberg for his excellent technical assistance.

SUMMARY

The distribution of cesium 137 in sections through whole male and pregnant female mice has been investigated by autoradiography at different times after injection.

ZUSAMMENFASSUNG

Die Verteilung von Caesium 137 ist in Schnitten durch ganze männliche und gravide weibliche Mäuse zu verschiedenen Zeitpunkten nach der Injektion autoradiographisch untersucht worden.

RÉSUMÉ

Les auteurs ont étudié la distribution du caesium 137 sur des coupes totales de souris males et de souris femelles gravides par autoradiographie à différents intervalles après l'injection.

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FROM THE INSTITUTE OF RADIOPHYSICS (DIRECTOR: PROF. R. M. SIEVERT), KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN.

CESIUM 137 AND ITS GAMMA RADIATION IN TELERADIOTHERAPY

by

R. THORAEUS

Up till now more than one thousand radioactive isotopes have been artificially produced, and the properties of their radioactivities are fairly well known. Among them, however, only a very few have attracted interest as regards radiotherapy application. One of these few is Cs^{137}, and the reasons for it holding such a position are undoubtedly the monoenergetic gamma radiation emitted, and its comparatively long half-life (Cs^{137} has by far the longest useful life of any of the artificially produced gamma radiating isotopes available in large quantities). There are, however, certain disadvantages in its use.

Cs^{137} was discovered during the late 1940's; by 1950 the characteristics of its radioactivity were fairly well known, and the possibilities of separating sufficient amounts were under investigation. It is well known that this isotope is produced by fission of U^{235} in the uranium fuel rods of atomic energy reactors. The fission products are accumulated in the fuel rods and must be removed from the fuel periodically to maintain efficiency. Cs^{137} is thus a true waste product. The rapid development of nuclear reactors is now expected to make available large quantities of this material at a relatively low price in the near

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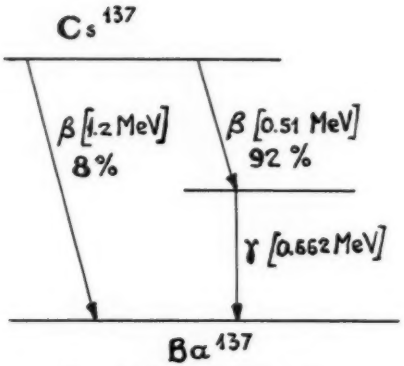

Fig. 1. Radioactive decay of Cs^{137}.

future. BRUCER seems to have been the first to have discussed thoroughly the problems of radiotherapy by means of Cs^{137} gamma radiation from kilocurie sources (1, 2, 3, 4). He has characterized this isotope as 'a very important radiation source for future radiotherapy'.

Radioactivity characteristics of Cs^{137}

We shall briefly review the available information as concerns the most important characteristics of Cs^{137} radioactivity.

Cesium is not chemically stable in its metallic form and must therefore be produced in the form of a chemical compound with the requisite stability from both the chemical and radiation aspects. For example, the nitrate cannot be used because it decomposes under the influence of intense radiation. At present Cs^{137} material is commercially available in two chemical forms, $CsCl_2$ and $CsSO_4$.

In the USA, radioactive cesium is produced at Oak Ridge as dry cesium chloride powder. This powder is then pressed to form compact pellets with a density of about 3.3 g/cm³, containing 22 curies of Cs^{137} per gram of solid. The pellets are made in various diameters and doubly enclosed in welded stainless steel capsules.

In the United Kingdom radioactive cesium is produced at Harwell and Amersham as cesium sulphate. This also is pressed into pellets to provide gamma radiation sources. The specific activity is in the region of 18 curies per gram of cesium sulphate and the density of the compressed salt is approximately 3 g/cm³. The pellets are doubly encapsulated, first in a 10 % iridium-platinum liner which in turn is contained in a Monel metal source holder, both being sealed with a hard silver solder.

The radioactive pellet must fit into the source holder closely enough not to

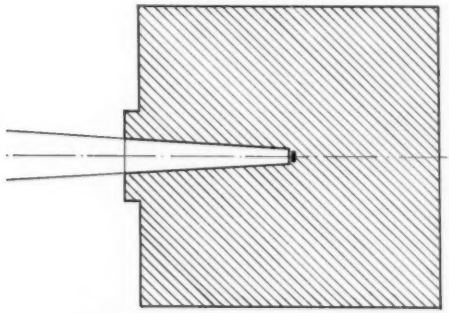

Fig. 2. Schematic presentation of the cylindric lead container housing the cesium source.

move when the source is subjected to vibration. All sources must be rigorously tested to ensure freedom from leakage and from surface contamination.

The radioactive decay is shown in Fig. 1. Cs^{137} emits beta particles with energies of 1.2 and 0.51 MeV. The latter beta emission results in an excited state of Ba^{137} which in turn decays to its stable state in emitting a monoenergetic gamma radiation of 0.662 MeV energy. The beta emission occurs to 92 % via the excited state, and 8 per cent directly to the stable state. The decay from the excited state occurs to 89 % as gamma radiation, and the remainder as internal conversion electrons.

The half-life of Cs^{137} is stated to be 30 ± 3 years. This means that the decay rate is approximately 1.5 % per year. As far as radiotherapy is concerned, decay corrections of the dose rate may thus be spaced at, at least, one year periods.

As already mentioned, the specific activity of the salt is about 20 curies per gram. Due to the production process of Cs^{137} the figures mentioned are considered as maximum values which cannot at present be increased. Comparing some of the most important radioactivity characteristics of Cs^{137} and Co^{60}, it is of particular interest to note that the gamma emission in rhm per curie of cobalt 60 is about 3.5 times as high as that of Cs^{137}, and further that a considerable increase in specific activity of the Canadian Co^{60} material, from 35 curies per gram in 1956 to a maximum of about 150 at present, has occurred.

Due to the relatively low specific activity it is not possible to produce kilocurie sources of Cs^{137} material with such small diameters as for example those of Co^{60} (1.5 to 2 cm). The dimensions of a Cs^{137} source for a given radiation output will thus be large compared with Co^{60}. For example, a 1 000 curie Cs^{137} gamma source will be 2.5 to 3.0 cm in diameter and 3 to 4 cm in height.

The long half-life of Cs^{137} is a great advantage, but it is usually accepted without regard to the Cs^{134} isotope which is produced by the same process and

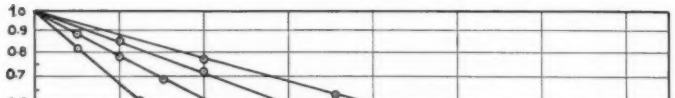

Fig. 3. Attenuation measurements for HVL determinations.

thus exists more or less as a component in the radioactive cesium material. This component has a much higher gamma radiation emission per curie than Cs^{137}, but a correspondingly much shorter half-life, about 2.3 years, and is therefore usually considered as a contamination in the radioactive material.

Cs^{134} gamma radiation is not monoenergetic, but has a number of energies, some of which are not very far from that of Cs^{137}. There is, however, also a small amount of gamma component the energy of which is practically the same as that of cobalt 60. A contamination by Cs^{134} will thus hardly impair the quality of the radiation from a therapeutic point of view. But the important effects to be expected during the first years are a more rapid decrease of the exposure dose rate, and a temporarily somewhat higher rate of leakage radiation through the protection barriers, particularly that of the source head.

It is said that the Cs^{134} contamination in new cesium sources may amount to as much as 15 %, but usually it is much lower, some 5 to 8 %, or less. In the case of considerable contamination the first half-life of the material will never reach the 30 years value expected from Cs^{137}, but will occur far short of this value. In fact, the first half-life of such a cesium source may not be significantly greater than that of a cobalt 60 source.

Radiation measurements

As the clinical use of Cs^{137} gamma radiation is expected to be introduced at Radiumhemmet quite soon, and as the first and fundamentally most important prerequisite for a proper clinical use of an ionizing radiation is its correct measurement, it was considered to be a matter of importance to study the properties of this radiation in advance. A point of particular interest in this connection is the fact that the gamma radiation emitted is monoenergetic.

The cesium gamma radiation used in this investigation was obtained from a source the age of which was about 8 years. This means that the influence of

Table 1

HVL of Cs^{137} gamma radiation

Reference	mm Cu	mm Pb	cm water	cm Al
N S Circular 583 (1957)				
alculated	10.8	5.8	8.1	3.4
xperimental	10.9	5.6		
H YBITTLE and DALLISON (1958)	10.6	5.4	8.0	—
R diations from radioactive atoms 1959)	—	6.0	8.0	—
B RNS et coll. (1959)	10.9	5.3	7.8	—
T ORAEUS (1959 to 1960).....	11.0	5.8	8.2	3.5

an y initial contamination by Cs^{134} had been essentially eliminated by its own decay. The gamma radiation used was thus substantially that emitted by Cs^{137}. The source was about 2 mm in diameter and housed in a cylindric lead container, as shown schematically in Fig. 2. The lead thickness was at least 9 cm, i. e. about 15 half-value layers, in all directions around the beam.

The radiation measurements were made using our substandard, the properties of which have been described elsewhere (11, 16). The energy dependence is small enough to permit of such radiation measurements as are required for the satisfactory determination of half-value layers. A half-value layer determined in this way can then be used to interpolate the corresponding calibration factor, by which the measurements can be given in terms of the roentgen.

In the case of a low exposure dose rate it is of great value to be able to increase the sensitivity of the instrument. This can be accomplished by removal of the additional capacitor, thus reducing the electrostatic capacitance. In this way the response of the substandard unit to radiation is increased nearly five times. The calibration factors for this version of the substandard instrument show the same small percentage change with radiation quality as the complete instrument.

Attenuation measurements of Cs^{137} gamma radiation under narrow-beam conditions were made in lead, copper, water, and aluminium. The attenuation data are plotted in the semilogarithmic diagram shown in Fig. 3. It appears from the diagram that the measurement results fit closely to straight lines, as might have been theoretically expected in the case of a monoenergetic radiation. The half-value layers interpolated from the experimental results are: 11.0 mm of copper, 5.8 mm of lead, 8.2 cm of water, and 3.5 cm of aluminium. These values are compared in Table 1 with some values collected from other recent papers. It appears that the agreement between the author's results and those obtained from the NBS Circular 583 (9) is very good, in most cases being almost within the measuring accuracy of the substandard.

Measurements of Cs^{137} gamma radiation can accordingly be made with a

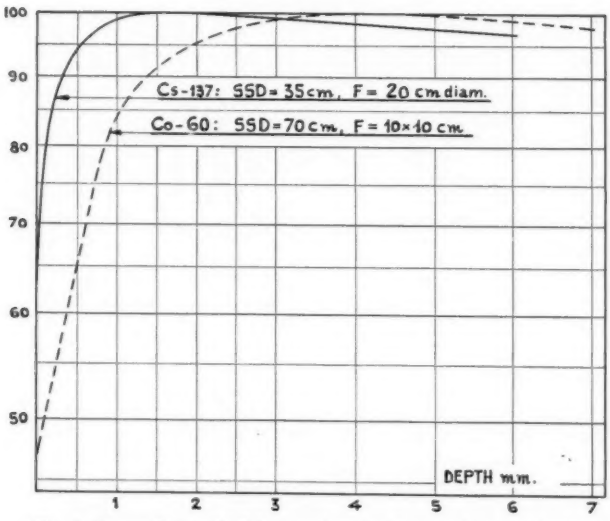

Fig. 4. Comparison of build-up regions for Cs^{137} and Co^{60} radiations.

reliable ionization chamber unit, provided it has a small energy dependence over a wide range of half-value layers, and is satisfactorily calibrated to such an extent that the factor for cesium radiation can be directly obtained, or safely interpolated in the calibration diagram.

Clinically important properties

In studying the percentage penetration of Cs^{137} gamma radiation into the human body, the question of build-up is of primary interest. The existence of a build-up region means a corresponding skin-sparing effect which is of a great value in clinical work. HAYBITTLE and DALLISON (10) have recently investigated this question by measurements at a source-skin distance of 35 cm. They found that (1) their beam was considerably contaminated with secondary electrons, (2) these electrons were effectively removed by a 0.5 mm thick filter of stainless steel, and that (3) maximum ionization with the filtered gamma radiation was attained at a depth of about 1.4 mm in tissue equivalent material.

This result indicates that the build-up effect of Cs^{137} gamma radiation is comparatively small. The skin-sparing effect obtained with this radiation is thus substantially less than that obtained with Co^{60} gamma radiation; in the case of the latter this effect is of paramount clinical importance. To get a direct comparison, the build-up regions of both Cs^{137} and Co^{60}, obtained from

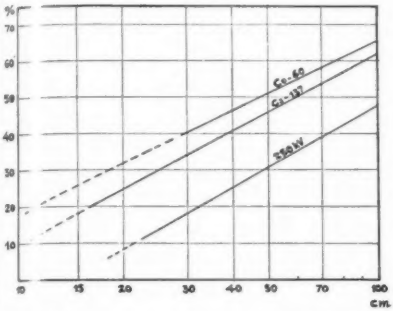

Fig. 5. Comparison of percentage depth dose at 10 cm depth using three different radiations.

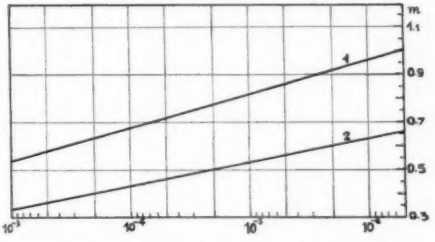

Fig. 6. Attenuation factors for Cs^{137} gamma radiation in different thicknesses of ordinary concrete (1) and iron-ore concrete (2).

the references 10 and 11, have been plotted in the diagram shown in Fig. 4. It appears that the depth of the build-up region of Co^{60} is about three times greater than that of Cs^{137}.

Considerations of the physical and radiation properties, particularly the comparatively low specific activity, seem at present to indicate certain limitations such that Cs^{137} radiation may be expected to be most suitable for those types of therapeutic application in which moderate focal distances of 20 to 35 cm are used. A similar opinion has recently been stated by JOHNS (12) from his experience with a 1 300 curie source.

However, at such short focal distances as those below 35 cm, the high penetration of the radiation cannot be appropriately utilized to produce its best possible percentage depth doses. BRUCER (4) has studied the central axis percentage depth dose at 10 cm depth in water as a function of the source-skin distance, using three different radiations. All the beams were defined by a fixed field size of 4×6 cm at a distance of 30 cm from the source. The results are shown in Fig. 5, and refer to the radiations Co^{60} gamma, Cs^{137} gamma, and 250 kV constant potential roentgen radiation.

In the current literature there have as yet been very few observations published as regards the biologic reactions produced in the human skin and tissues by cesium 137 gamma radiation. COMAS and BRUCER (6), however, have recently reported their first impressions of therapy with this radiation, using a kilocurie teletherapy machine at the Medical Division of the Oak Ridge Institute of Nuclear Studies. This machine consists essentially of a shielded 1 500 curie cesium 137 source, capable of movement in four directions: tilt, vertical, horizontal, and circular. Very short collimator-skin distances can be used in setting up stationary portals. Most patients were treated at a distance of 29 cm between the collimator and the centre of rotation, and a distance of 60 cm between the source and the centre of rotation. The radiation output was 15 r/min at 60

Table 2

Comparison of penetration in various materials

Attenuation factor	Attenuator material	Thickness of attenuator	
		Cs^{137} gamma	1.4 MV roentgen
0.5 (first HVL)	Water	8.2 cm	8.3 cm
— „ —	Al	3.5 cm	3.6 cm
— „ —	Cu	11.0 mm	10.8 mm
10^{-3}	Iron-ore concrete	35 cm	33 cm
10^{-4}	— „ —	43 cm	43 cm
10^{-5}	— „ —	53 cm	52 cm
10^{-6}	— „ —	63 cm	62 cm

cm, and the diameter of the source was 3 cm, giving an extensive penumbra that limited the concentrating effect of both the moving beam and multiple port techniques.

The skin reactions observed were found to be similar to those occurring with cobalt 60 gamma radiation, except that in the case of cobalt the reactions usually occurred later. The erythema produced by Cs^{137} gamma radiation was usually observed with a skin dose of approximately 2 000 r around the third or fourth week of treatment. From the preliminary indications it would appear that a higher dose in comparison to cobalt 60 therapy can be given without the occurrence of excessive skin reactions, except around the mouth and pharynx where no difference was noted in the timing, intensity, and the character of the reactions, as compared with those in 250 kV roentgen therapy or cobalt 60 therapy.

Penetration and Protection

The most frequently used material for protection against high energy radiation is ordinary concrete. Its density can be raised to about 2.4 by use of a mechanical treatment, called vibration. The only disadvantage of this material is the comparatively great thicknesses required at radiations of high energy. To reduce this disadvantage the use of iron-ore concrete was introduced into the radiation protection technique by SIEVERT (13) in 1933. In a later paper (17) the present author has described the modern production and properties of this high grade material from experience gained over the last few years. Subjecting this material also to vibration, a density of 3.8 has been obtained. A survey of the attenuation of Cs^{137} gamma radiation in different thicknesses of these two types of concrete is given in Fig. 6. Curve 1 refers to ordinary 2.4-concrete and curve 2 to 3.8-iron-ore-concrete.

As pointed out by BRUCER (4), an interesting advantage of Cs^{137} gamma radiation is that although the attenuation in substances of low atomic numbers

present in the human body is only 30 % greater than for Co^{60}, the attenuation in substances of high atomic numbers used as protective material in the housing (source head) is 80 % greater than for Co^{60}. Thus, although the penetration in the human body is not much reduced, the problem of shielding the primary beam is notably reduced with Cs^{137}. Due to this, lead shielding and collimating is relatively more effective for gamma radiation from Cs^{137} than for that from Co^{60}. In many cases where cesium sources are being considered lead lining can thus be used to advantage. A cesium source can, in fact, be housed in a shield, the thickness of which is only two-thirds of that required for a cobalt source of the same radiation output.

The 'equivalence' between a monoenergetic radiation and a roentgen radiation consisting of a continuous range of radiation component energies, a so-called 'bremsstrahlung', is sometimes considered; this equivalence is then usually referred to the penetration. It is evident, however, that no real equivalence exists, but a comparison may nevertheless be of interest and can be made without objection provided no particular conclusions are drawn from the results.

Some results have been obtained using the half-value layers given above. Further results were given in a separate paper (17) in which the author has shown the special type of attenuation curves that are suitable for study of equivalence in penetration. Using such curves it was possible to compare the attenuation in 3.8-iron-ore-concrete of the monoenergetic gamma radiation from Cs^{137} with that of roentgen radiation of various peak energies. The results have been collected in Table 2 and show that in this region of attenuation Cs^{137} gamma radiation has very nearly the same penetration as a roentgen radiation of 1.4 MV peak energy. As far as penetration is concerned they may thus be considered 'equivalent' in the region investigated. It appears that the agreement is very good. The region of attenuation factors 10^{-3} to 10^{-6} is of direct interest in radiation protection techniques.

Conclusions

From the review now given and on the basis of the measurement results reported upon the following conclusions may be drawn.

1. Due to the origin of Cs^{137} there are at present no practical means available to produce a material of very high specific activity; the maximum values seem to be about 20 curies per gram, and a salt density of about 3 g/cm³. This means that sources of a suitable size for teletherapy can only be used at the comparatively short treatment distances of 15 to 35 cm. At such distances, however, the penetrating power of the radiation cannot be fully utilized to produce its highest possible percentage depth doses. There seem to be relatively few applications in which a short treatment distance would be desirable for its own sake.

2. The general opinion appears to be that the clinical use of Cs^{137} is limited

but that on the other hand its radiation may be well suited for head and neck applications particularly when the dimensions of the source head must be kept as small as possible. The use of tungsten heavy alloy (density about 18), or of uranium, may then be considered.

3. The build-up effect of Cs^{137} gamma radiation is comparatively small, particularly when small source-skin distances are used. The skin-sparing effect of this radiation is, therefore, substantially less than that of Co^{60} gamma radiation; such an effect is in fact one of the big advantages of the latter.

4. The measurement of Cs^{137} gamma radiation can be done by means of a reliable ionization chamber unit with a small energy dependence over a wide range of half-value layers, provided it has been subjected to a reliable calibration such that the factor for the cesium gamma radiation can be directly obtained, or safely interpolated in the calibration diagram.

5. One advantage of Cs^{137} gamma radiation is that less room protection is required than for a comparable Co^{60} unit. The primary beam requires only about two-thirds the thickness of shielding of the cobalt-60 source. Furthermore, lead lining can be used to advantage since lead is relatively more effective for Cs^{137} radiation than for Co^{60} radiation.

6. The question of Cs^{134} contamination in the radioactive material of a cesium source is primarily of an economical nature and should thus be carefully considered. When a cesium source is to be ordered, it is recommended that a request be made for a guarantee of the percentage decay occurring in the first and second 5-year periods. This guarantee may then be compared to calculations based on a half-life of 30 years. In case of considerable Cs^{134} contamination, a temporarily somewhat higher rate of leakage radiation through the protection barriers, particularly that of the source head, is also to be expected.

SUMMARY

A review of the characteristics of cesium radioactivity, including partial comparison with that of cobalt is given. The measurement of cesium gamma radiation by means of an extensively calibrated substandard is described and the experimental results, particularly the half-value layers of some materials, are presented. Certain clinically important properties of the radiation, the radiation protection using radioactive cesium, and the result of a determination of the peak energy of the roentgen radiation equivalent in penetration to the cesium gamma radiation, are discussed.

ZUSAMMENFASSUNG

Es wird eine Übersicht über die charakteristischen Eigenschaften der Radioaktivität von Cesium gegeben, und sie werden teilweise mit denen von Kobalt verglichen. Die Messung der Cesium-Gamma Strahlung mittels eines umfassend geeichten Substandards wird beschrieben, und experimentelle Ergebnisse, besonders die Halbwertschichten von gewissen Materialen, werden gezeigt. Gewisse klinisch wichtige Eigenschaften und der Strahlenschutz bei Verwendung von radioaktivem Cesium sowie das Ergebnis der Bestimmung des Scheitelwertes der Röntgenstrahlung, die in Bezug auf Durchdringungsvermögen die Cesium-Gamma-Strahlung äquivalent ist, werden diskutiert.

RÉSUMÉ

L'auteur rappelle les caractéristiques de la radioactivité du césium et en donne une comparaison partielle avec celle du cobalt. Il décrit la mesure de la radiation gamma du césium au moyen d'un étalon secondaire dûment étalonné et présente des résultats expérimentaux, en particulier les couches de demi-absorption de certaines substances. Il étudie certaines propriétés de cette radiation qui sont importantes pour la clinique, la question de la radioprotection contre le césium radioactif, et le résultat de la détermination de l'énergie de pointe de la radiation roentgen équivalente en pénétration à la radiation gamma du césium.

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BOOK REVIEWS

RISA Encephalography and Conventional Neuroradiologic Methods. A Comparative Study. By Giovanni Di Chiro. 102 pages, 38 illustrations, 6 tables, 60 sketches, 3 diagrams. Acta radiol. (1961) Suppl. No. 201. Price: Sw. Kr. 35: —.

Conventional neuroradiologic methods (ordinary skull roentgenograms, pneumography and angiography) are highly accurate for the detection and localization of intracranial lesions but not equally precise in determining the extent of the lesions. Pneumography and cerebral angiography carry a low but definite incidence of morbidity and mortality, and are a cause for discomfort to the patient. It is therefore important to strive to find new diagnostic procedures.

Collimated radioactive scintillation scanning of the head with RISA (radio-iodinated serum albumin) has been used in more than 600 patients at the National Institute of Neuroradiological Diseases and Blindness (NINDB) to obtain information relative to the presence, location and extension of cranial lesions. To assess the reliability of this new method, the results of examinations with RISA were compared with the results of conventional neuroradiologic studies in a series of verified cranial lesions.

Tumoral lesions of the glioma group and in particular 'early' and 'infiltrating' gliomas missed by neuroradiology were detected with RISA. Conversely, some intracranial lesions, detected by the conventional neuroradiologic methods were missed by RISA. The latter was least helpful in cases of intra-, suprasellar and midline posterior fossa lesions. Lesions situated laterally in the posterior fossa, such as acoustic neuromas, could on the other hand frequently be detected by RISA. In determining the extent of some gliomas and occasionally also of other types of lesions, RISA is sometimes more accurate than conventional neuroradiologic procedures. The multiplicity of certain lesions (metastases, meningiomas) which occasionally escapes the neuroradiologic methods is established with RISA. At least at present, however, a certain degree of unpredictability is involved with the use of RISA since even large lesions may sometimes unexplainably be missed.

Conventional neuroradiology remains unmatched for assessing the nature of the different lesions, however.

The procedure of RISA-encephalography is harmless, causes no discomfort to the patient and (after the initial expenditure) is not costly. Because of the amount of information it offers, RISA-encephalography should not be regarded as a mere preliminary screening procedure. It has the fullest qualifications for membership among the neuroradiologic methods and should be used as a complement to these.

Autoreview

ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS. Volume VII. Edited by C. A. Tobias and J. H. Lawrence. 362 pages, 88 illustrations and 10 tables. Academic Press, New York 1960. Price: $ 10.

The present volume presents, like the preceding ones, detailed reviews with extensive bibliographies of recent developments within selected sections of the vast domain of biophysics. It also resembles the earlier volumes in that a large part of the space is dedicated to the uses of radiation and radioisotopes in research and to various radiation effects.

The first paper, by G. S. Stent and C. R. Fuerst, deals with the genetic and physiologic effects of radiophosphorus incorporated in viruses and bacteria. It describes a number of beautiful experiments leading to the at first sight astonishing result that the effects considered are not primarily ordinary radiation effects of beta rays but effects caused by the disruption of DNA molecules when phosphorus atoms in the molecules are transformed into recoiling sulphur atoms.

In the next paper, by D. Carlström, apparatus and methods for roentgen-diffraction structure analysis on a microscale are described and examples of medical applications are given. J. H. Taylor writes on autoradiography with tritium; this contribution is noteworthy for the great resolution of the excellent films, in which the activity in single chromosomes can be studied. L. E. Lipetz reviews the electrical and chemical phenomena following optical or electrical stimulation of facet eyes of horseshoe crabs, which for technical reasons are suitable for such studies. The bearing of the results for an appreciation of corresponding processes in the eyes of higher animals and man is discussed.

A paper by N. N. Livshits on the physiologic effects of radiation on the central nervous system is of particular interest. Mainly but by no means exclusively on the basis of Russian work, various effects, such as changes in conditioned and unconditioned reflexes, EEG, and the metabolism of different substances, are reported in detail. The central nervous system appears to be considerably more sensitive to radiation than was earlier assumed, and in many cases unexpectedly low doses may produce significant effects.

D. Gitlin and C. H. Janeway write on isotope studies of plasma proteins with emphasis on their own work with radio-iodine. These experiments concern the diffusion of proteins between extra- and intravascular spaces and their degradation under normal and pathologic conditions. The last paper, by L. W. Law, deals with radiation carcinogenesis, a subject of great topical interest due to the general concern over the possibly evil effects of radioactive fall-out and the medical use of roentgen radiation. The author clearly shows the great difficulties in arriving at a well-founded opinion in these matters and rightly criticizes the bold statements often scattered about.

While containing much more biology and medicine than physics the book should still prove most useful also to physicists interested in the subjects treated.

Sven Benner

ERGEBNISSE DER WIRBELSÄULENFORSCHUNG. Ausgegeben von H. Junghanns. 140 Seiten, 100 Abbildungen. Hippokrates-Verlag, Stuttgart 1960. Price: DM 33.

The book consists of papers of a congress and deals with the results of various investigations. Biochemical and biophysical investigations of the intervertebral cartilages, the production of congenital deformities of vertebrae by experimental influences during foetal life (lack of oxygen, roentgen irradiation), and movement studies of the cervical spine are among the subjects presented. The results of advanced research are concerned more with the biology and pathology of the spine and not with clinical roentgen diagnostics.

Folke Knutsson

RADIATION INJURY IN MAN. ITS CHEMICAL AND BIOLOGICAL BASIS. PATHOGENESIS AND THERAPY. By E. P. Cronkite and V. P. Bond. 200 pages and 18 illustrations. Charles C. Thomas, Springfield Ill. 1960. Price: $ 6.50.

The aim of this book: 'to fill a current need for a semi-technical or non-technical presentation of basic and practical material necessary for an understanding of the effects of ionizing radiation in man' is admirably fulfilled. The design is the usual one: basic physical and chemical information in introductory chapters followed by biologic and medical aspects. The language is plain and descriptive, mathematical formulas being avoided and technical terms explained in a glossary.

The symptoms of irradiation injury are a function of the radiation dose, and any therapeutic measures are dependent on the dose received. These facts are thoroughly discussed in chapters entitled: 'The clinical picture of acute irradiation injury in man' and 'Diagnosis and therapy of human radiation injury; practical considerations'. These are most useful by reason of the clinical approach which is not often found in current textbooks. The authors discuss genetic and long term effects, as well as the difficult question of the estimation of risks from fall-out activity. These are fields where the most divergent opinions have been expressed, even by scientists. Some of the difficulties arise because the statistical significance of biologic effects from low-level radiation is in most cases low, and the interpretation of the results is often open to question. The authors wonder, however, and probably rightly, whether disagreements may not also partly be occasioned by emotional, political and diplomatic considerations.

A. Forssberg

URETHROGRAPHIC STUDIES OF PROSTATIC TUBERCULOSIS. By Niels Bentzen. Thesis. 114 pages and 45 illustrations. Aarhuus Stiftsbogtrykkerie, Copenhagen, Denmark.

The book is a thesis for a doctorate. The title covers only about half the contents, as detailed consideration is also given to relationship of renal tuberculosis to prostatic tuberculosis, the role of the prostate in tuberculous bacilluria, the treatment of prostatic tuberculosis, and the pathogenesis of male genito-urinary tuberculosis.

The urethrographic studies comprise 155 cases of tuberculous bacilluria and a normal control series of 7 cases. Exposures were made during and after injection, and during micturition.

Abnormal filling of the prostate was found in 126 of the cases. The cavities, and possibly the ducts, were filled in 99 cases while in the remaining 27 cases only the ducts were demonstrated. As the author emphasizes, these findings do not necessarily indicate tuberculosis and the final interpretation must be based on the history and the clinical signs. The follow-up studies, carried out during chemotherapy, demonstrated a considerable improvement in the appearances although these never completely returned to the normal. The illustrations adequately fulfill their purpose.

The genetic radiation hazards involved in urethrography are considered. These were found to be of only slight importance in the series under review, as the majority of the patients were over 40 years of age, and 38 per cent of them had a history of bilateral tuberculous epididymitis.

In a general consideration of genito-urinary tuberculosis, the author expresses the opinion that prostatic, like renal, involvement is a hematogenic phenomenon and of rather a different character from a direct spread to the ureter or bladder.

Nils P. G. Edling

RADIATION BIOLOGY. Proceedings of the Second Australasian Conference in Radiation Biology, Melbourne 15—18 December 1958. Editor J. H. Martin. 304 pages, 86 illustrations and 50 tables. Butterworths Scientific Publications, London 1959. Price: 69 Shillings.

It has become almost a habit to print the proceedings of conferences in bookform. Oversaturation is imminent since scientific progress can hardly keep pace with the rate of publishing. This statement should not restrain prospective purchasers of this book since it contains stimulating lectures and discussions on important problems of current research.

Although most branches of radiobiology and allied sciences were represented in the conference program, two or three main themes predominated. Two experienced radiobiologists were invited to give four lectures each; this afforded the opportunity for a comprehensive treatment of their subjects to be made.

L. F. Loutit from Harwell gave a well documented account of the radiation induction and treatment of leukaemia as well as the related fields of bone marrow transfer and its immunologic aspects. This is a balanced and careful account of our knowledge which clearly sets out the many unsolved problems. The present situation is that we cannot exclude the possibility that the experimental production of leukemia in animals is dose rate dependent and that high dose rates produce a higher yield of leukemia. Mole, as quoted by Loutit states: '. . . there is no evidence to support the hypothesis that the chief determining factor in the incidence of radiation-induced leukemia is dose; and that there is some evidence from existing human data which denies the validity of extrapolation on the relation between dose and leukemia to situations where the dose intensity is very much less'. Two other lectures given by Loutit were devoted to the radioactive strontium problem and other radioactive isotopes in the food chain.

What may be called basic radiobiology is another theme, admirably treated by L. H. Gray. Two of his lectures centred around the influence of oxygen on radiosensitivity and in the second he discussed future experimental possibilities which have been opened up by recent technical advance, particularly the analyses of free organic radicals by electron spin resonance spectroscopy.

The book consists of 29 lectures and discussions in all, which also cover radiation chemistry, genetics and protection.

A. Forssberg

THE CELL NUCLEUS. Proceedings of the 1959 Meeting at the University of Cambridge by the Faraday Society. Editor J. S. Mitchell. 269 pages, 115 illustrations and 38 tables. Butterworths, London 1960. Price: 50 Shillings.

The nucleus exerts a fundamental control of cellular function. The mechanism by way of which this is maintained constitutes problems which need the joint cooperation of specialized workers in the fields of biophysics, chemistry and the classical biologic sciences. The present contributions to our understanding of this subject are the proceedings of an informal meeting at Cambridge. The book is certainly one which requires a good deal of knowledge on the part of the reader; the participants are leading workers in various relevant fields and the presentation of the material, in short lectures and discussions, is that of the specialist talking to fellow specialists in adjacent fields.

In recent years great advances have been made towards a better understanding of the structure of chromosomes and the mechanism of the synthesis of the key substance, deoxyribonucleic acid (DNA). The papers given at the conference centre round these and similar matters. The reader obtains a fairly comprehensive view of the structure of the nucleolus and

its function in mitotic and metabolic activities. Aspects of the synthesis of nucleic acids and the effects of irradiation on this process, with particular reference to the autoradiographic technic, as well as models of DNA structure as shown by various biophysical analyses, are all discussed. Occasionally the reader is faced with accounts of bold attempts to open quite new fields of research, as for example the cultivation of nuclei and chromosomes in vitro.

In all, the book offers stimulating reading about the basic aspects of life.

A. Forssberg

DIE ASBESTOSE DER LUNGEN. Genese — Klinik — Röntgenologie. Von H. Bohlig, G. Jacob und H. Müller. 166 Seiten, 97 Abbildungen. Georg Thieme, Stuttgart 1960. Price: DM 56.

This monograph is probably the most comprehensive and detailed analysis of asbestosis ever published and, as indicated in the title, deals with the genesis, clinical aspects, and roentgenology of the disease, in addition to which the pathology and histology are described. The chapter on the roentgenology of asbestosis forms the largest section of the book as might be expected. The attempt to achieve a satisfactory division of the condition into stages is perhaps of greatest interest but it cannot be said that the authors have entirely succeeded. Although they are in general agreement with Saupe's four-stage division they state plainly that the first stage (0—I) is more or less impossible to diagnose and that the next stage (I) also causes great difficulties. Stages II and III, on the other hand, may readily be determined from the roentgen findings with due consideration to the occupational history. The division into stages is based wholly on the changes in the pulmonary parenchyma. The pleural reaction is apparently considered by these authors to be one of the complications of the disease in spite of their observation that pleura thickening is observed post mortem in nearly all cases, even in those with mild asbestosis (»Bei den Sektionsfällen wurden auch schon bei leichten Asbestosen fast ausnahmslos die Pleuraverschwartungen bestätigt«). It would appear to the reviewer that pleural reaction is a significant part of the clinical entity and produces disturbance of pulmonary function at an early stage; the thickened pleura causes 'constrictio pulmonum' with reduction of ventilation. If this fact is not taken into consideration it is hardly possible to correlate the roentgenologic and clinical signs. A division into stages on the principles followed by Saupe and the present authors is consequently of little practical value.

The illustrations are of high quality but again the pleural changes are not sufficiently emphasized. With the reservation mentioned, which affects only a relatively small part of the contents, the book is warmly recommended as a mine of information.

Gunnar Jönsson